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(54) Title: TRANSCRIPTION FACTORS

(57) Abstract: The invention provides human transcription factors (TRFX) and polynucleotides which identify and encode TRFX. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of TRFX.

TRANSCRIPTION FACTORS

TECHNICAL FIELD

This invention relates to nucleic acid and amino acid sequences of transcription factors and to the use of these sequences in the diagnosis, treatment, and prevention of cell proliferative, autoimmune/inflammatory, neurological, and developmental disorders, and in the assessment of the effects of exogenous compounds on the expression of nucleic acid and amino acid sequences of transcription factors.

BACKGROUND OF THE INVENTION

Multicellular organisms are comprised of diverse cell types that differ dramatically both in structure and function. The identity of a cell is determined by its characteristic pattern of gene expression, and different cell types express overlapping but distinct sets of genes throughout development. Spatial and temporal regulation of gene expression is critical for the control of cell proliferation, cell differentiation, apoptosis, and other processes that contribute to organism development. Furthermore, gene expression is regulated in response to extracellular signals that mediate cell-cell communication and coordinate the activities of different cell types. Appropriate gene regulation also ensures that cells function efficiently by expressing only those genes whose functions are required at a given time.

Transcriptional regulatory proteins are essential for the control of gene expression. Some of these proteins function as transcription factors that initiate, activate, repress, or terminate gene transcription. Transcription factors generally bind to promoter, enhancer, or upstream regulatory regions of a gene in a sequence-specific manner, although some factors bind regulatory elements within or downstream of the coding region. Transcription factors may bind to a specific region of DNA singly or as a complex with other accessory factors. (Reviewed in Lewin, B. (1990) Genes IV, Oxford University Press, New York, NY, pp. 554-570.)

The double helix structure and repeated sequences of DNA create topological and chemical features which can be recognized by transcription factors. These features include hydrogen bond donor and acceptor groups, hydrophobic patches, major and minor grooves, and regular repeated stretches of sequence which induce distinct bends in the helix. Typically, transcription factors recognize specific DNA sequence motifs of about 20 nucleotides in length. Multiple adjacent transcription factor-binding motifs may be required for gene regulation.

Many transcription factors incorporate DNA-binding structural motifs which comprise either α helices or ß sheets that bind to the major groove of DNA. Four well-characterized structural motifs are helix-turn-helix, zinc finger, leucine zipper, and helix-loop-helix. Proteins containing these

motifs may act alone as monomers or form homo- or heterodimers that interact with DNA.

The zinc finger motif, which binds zinc ions, generally contains tandem repeats of about 30 amino acids consisting of periodically spaced cysteine and histidine residues. Examples of this sequence pattern include the C2H2-type and the C3HC4-type zinc fingers, and the PHD domain. (Lewin, supra ; Aasland, R., et al. (1995) Trends Biochem. Sci 20:56 - 59.) Zinc finger proteins each contain an α helix and an antiparallel ß sheet whose proximity and conformation are maintained by the zinc ion. Contact with DNA is made by the arginine preceding the α helix and by the second, third, and sixth residues of the a helix.

The leucine zipper motif comprises a stretch of amino acids rich in leucine which can form an amphipathic α helix. This structure provides the basis for dimerization of two leucine zipper proteins. The region adjacent to the leucine zipper is usually basic, and upon protein dimerization, is optimally positioned for binding to the major groove. Proteins containing such motifs are generally referred to as bZIP transcription factors. The helix-loop-helix motif (HLH) consists of a short α helix connected by a loop to a longer α helix. The loop is flexible and allows the two helices to fold back against each other and to bind to DNA. The transcription factor Myc contains a prototypical HLH motif. Most transcription factors contain characteristic DNA binding motifs, and variations on the above motifs and new motifs have been and are currently being characterized (Faisst, S. and S. Meyer (1992) Nucl. Acids Res. 20:3-26).

Mutations in transcription factors contribute to oncogenesis. This is likely due to the role of transcription factors in the expression of genes involved in cell proliferation. For example, mutations in transcription factors encoded by proto-oncogenes, such as Fos, Jun, Myc, Rel, and Spi1, may be oncogenic due to increased stimulation of cell proliferation. Conversely, mutations in transcription factors encoded by tumor suppressor genes, such as p53, RB1, and WT1, may be oncogenic due to decreased inhibition of cell proliferation. (Latchman, D. (1995) Gene Regulation: A Eukaryotic Perspective, Chapman and Hall, London, UK, pp 242-255.)

Gene expression is also affected by chromatin-associated proteins. In the nucleus, DNA is packaged into chromatin, the compact organization of which limits the accessibility of DNA to transcription factors and plays a key role in gene regulation. (Lewin, supra, pp. 409-410.) The compact structure of chromatin is determined and influenced by chromatin-associated proteins such as histones, high mobility group (HMG) proteins, helicases, and chromodomain proteins. There are five classes of histones, H1, H2A, H2B, H3, and H4, all of which are highly basic, low molecular weight proteins. The fundamental unit of chromatin, the nucleosome, consists of 200 base pairs of DNA associated with two copies each of H2A, H2B, H3, and H4. H1 links adjacent nucleosomes. HMG proteins are low molecular weight, non-histone proteins that may play a role in unwinding

DNA and stabilizing single-stranded DNA. Helicases, which are DNA-dependent ATPases, unwind DNA, allowing access for transcription factors. Chromodomain proteins play a key role in the formation of highly-compacted, transcriptionally silent heterochromatin.

Many neoplastic disorders in humans can be attributed to inappropriate gene expression. Malignant cell growth may result from either excessive expression of tumor promoting genes or insufficient expression of tumor suppressor genes. (Cleary, M.L. (1992) Cancer Surv. 15:89-104.) Chromosomal translocations may also produce chimeric loci which fuse the coding sequence of one gene with the regulatory regions of a second unrelated gene. Such an arrangement often results in inappropriate gene transcription. The Wilms tumor suppressor gene product, WT1, is a protein containing a DNA-binding domain consisting of four zinc fingers and a proline-glutamine rich region capable of regulating transcription. (ExPASy PROSITE document PR00049.) Deletions of the WT1 gene, or point mutations which destroy the DNA-binding activity of the protein are associated with development of the pediatric nephroblastoma, Wilms tumor, and Denys-Drash syndrome. (Rauscher, F.J. (1993) FASEB J. 7:896-903.)

Certain proteins enriched in glutamine are associated with various neurological disorders including spinocerebellar ataxia, bipolar effective disorder, schizophrenia, and autism. (Margolis, R.L. et al. (1997) Human Genetics 100:114-122.) These proteins contain regions with as many as 15 or more consecutive glutamine residues and may function as transcription factors with a potential role in regulation of neurodevelopment or neuroplasticity.

The immune system responds to infection or trauma by activating a cascade of events that coordinate the progressive selection, amplification, and mobilization of cellular defense mechanisms. A complex and balanced program of gene activation and repression is involved in this process. Hyperactivity of the immune system as a result of improper or insufficient regulation of gene expression may result in considerable tissue or organ damage. This damage is well documented in immunological responses associated with arthritis, allergens, heart attack, stroke, and infections. (Harrison's Principles of Internal Medicine, 13/e, McGraw Hill, Inc. and Teton Data Systems Software, 1996.) In particular, a zinc finger protein termed Staf50 (for Stimulated trans-acting factor of 50 kDa) is a transcriptional regulator and is induced in various cell lines by interferon-I and -II. Staf50 appears to mediate the antiviral activity of interferon by down-regulating the viral transcription directed by the long terminal repeat promoter region of human immunodeficiency virus type-1 in transfected cells (Tissot, C. (1995) J. Biol. Chem. 270:14891-14898).

The generation of multicellular organisms is based on the induction and coordination of cell differentiation at the appropriate stages of development. Differential gene expression confers the distinct identities of cells and tissues throughout the body. Failure to regulate gene expression during

development could result in developmental disorders.

The discovery of new transcription factors and the polynucleotides encoding them satisfies a need in the art by providing new compositions which are useful in the diagnosis, prevention, and treatment of cell proliferative, autoimmune/inflammatory, neurological, and developmental disorders, and in the assessment of the effects of exogenous compounds on the expression of nucleic acid and amino acid sequences of transcription factors.

SUMMARY OF THE INVENTION

The invention features purified polypeptides, transcription factors, referred to collectively as "TRFX" and individually as "TRFX-1," "TRFX-2," "TRFX-3," "TRFX-4," "TRFX-5," "TRFX-6," "TRFX-7," "TRFX-8," "TRFX-9," "TRFX-10," "TRFX-11," "TRFX-12," "TRFX-13," "TRFX-14," "TRFX-15," "TRFX-16," "TRFX-17," "TRFX-18," "TRFX-19," "TRFX-20," "TRFX-21," "TRFX-22," "TRFX-23," "TRFX-24," "TRFX-25," "TRFX-26," "TRFX-27," "TRFX-28," "TRFX-29," "TRFX-30," "TRFX-31," "TRFX-32," "TRFX-33," "TRFX-34," "TRFX-35," "TRFX-36," "TRFX-37," "TRFX-38," "TRFX-39," "TRFX-40," "TRFX-41," "TRFX-42," "TRFX-43," "TRFX-44," "TRFX-45," "TRFX-46," "TRFX-47," "TRFX-48," "TRFX-49," "TRFX-50," "TRFX-51," "TRFX-52," "TRFX-53," "TRFX-54," "TRFX-55," "TRFX-56," "TRFX-57," "TRFX-58," "TRFX-59," "TRFX-60," "TRFX-61," "TRFX-62," "TRFX-63," "TRFX-64," "TRFX-65," "TRFX-66," "TRFX-67," "TRFX-68," "TRFX-69," "TRFX-70," "TRFX-71," "TRFX-72," "TRFX-73," "TRFX-74," "TRFX-75," "TRFX-76," "TRFX-77," "TRFX-78," "TRFX-79," "TRFX-80," "TRFX-81," "TRFX-82," "TRFX-83," "TRFX-84," "TRFX-85," "TRFX-86," "TRFX-87," "TRFX-88," "TRFX-89," "TRFX-90," "TRFX-91," "TRFX-92," "TRFX-93," "TRFX-94," "TRFX-95," "TRFX-96," "TRFX-97," "TRFX-98," "TRFX-99," "TRFX-100," "TRFX-101," "TRFX-102," "TRFX-103," "TRFX-104," "TRFX-105," "TRFX-106," and "TRFX-107." In one aspect, the invention provides an isolated polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. In one alternative, the invention provides an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:1-107.

The invention further provides an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having

at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. In one alternative, the polynucleotide encodes a polypeptide selected from the group consisting of SEQ ID NO:1-107. In another alternative, the polynucleotide is selected from the group consisting of SEQ ID NO:108-214.

Additionally, the invention provides a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. In one alternative, the invention provides a cell transformed with the recombinant polynucleotide. In another alternative, the invention provides a transgenic organism comprising the recombinant polynucleotide.

The invention also provides a method for producing a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. The method comprises a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding the polypeptide, and b) recovering the polypeptide so expressed.

Additionally, the invention provides an isolated antibody which specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107.

The invention further provides an isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of a) a polynucleotide sequence selected from the group

consisting of SEQ ID NO:108-214, b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). In one alternative, the polynucleotide comprises at least 60 contiguous nucleotides.

Additionally, the invention provides a method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). The method comprises a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and b) detecting the presence or absence of said hybridization complex, and optionally, if present, the amount thereof. In one alternative, the probe comprises at least 60 contiguous nucleotides.

The invention further provides a method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). The method comprises a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

The invention further provides a composition comprising an effective amount of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and a

pharmaceutically acceptable excipient. In one embodiment, the composition comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. The invention additionally provides a method of treating a disease or condition associated with decreased expression of functional TRFX, comprising administering to a patient in need of such treatment the composition.

The invention also provides a method for screening a compound for effectiveness as an agonist of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting agonist activity in the sample. In one alternative, the invention provides a composition comprising an agonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with decreased expression of functional TRFX, comprising administering to a patient in need of such treatment the composition.

Additionally, the invention provides a method for screening a compound for effectiveness as an antagonist of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting antagonist activity in the sample. In one alternative, the invention provides a composition comprising an antagonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with overexpression of functional TRFX, comprising administering to a patient in need of such treatment the composition.

The invention further provides a method of screening for a compound that specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence

selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. The method comprises a) combining the polypeptide with at least one test compound under suitable conditions, and b) detecting binding of the polypeptide to the test compound, thereby identifying a compound that specifically binds to the polypeptide.

The invention further provides a method of screening for a compound that modulates the activity of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107. The method comprises a) combining the polypeptide with at least one test compound under conditions permissive for the activity of the polypeptide, b) assessing the activity of the polypeptide in the presence of the test compound, and c) comparing the activity of the polypeptide in the presence of the test compound with the activity of the polypeptide in the absence of the test compound, wherein a change in the activity of the polypeptide in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide.

The invention further provides a method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence selected from the group consisting of SEQ ID NO:108-214, the method comprising a) exposing a sample comprising the target polynucleotide to a compound, and b) detecting altered expression of the target polynucleotide.

The invention further provides a method for assessing toxicity of a test compound, said method comprising a) treating a biological sample containing nucleic acids with the test compound; b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of i) a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, ii) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, iii) a polynucleotide sequence complementary to i), iv) a polynucleotide sequence complementary to ii), and v) an RNA equivalent of i)-iv). Hybridization occurs under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological

sample, said target polynucleotide comprising a polynucleotide sequence selected from the group consisting of i) a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, ii) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214, iii) a polynucleotide sequence complementary to i), iv) a polynucleotide sequence complementary to ii), and v) an RNA equivalent of i)-iv). Alternatively, the target polynucleotide comprises a fragment of a polynucleotide sequence selected from the group consisting of i)-v) above; c) quantifying the amount of hybridization complex; and d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

BRIEF DESCRIPTION OF THE TABLES

Table 1 shows polypeptide and nucleotide sequence identification numbers (SEQ ID NOs), clone identification numbers (clone IDs), cDNA libraries, and cDNA fragments used to assemble full-length sequences encoding TRFX.

Table 2 shows features of each polypeptide sequence, including potential motifs, homologous sequences, and methods, algorithms, and searchable databases used for analysis of TRFX.

Table 3 shows the tissue-specific expression patterns of each nucleic acid sequence as determined by northern analysis; diseases, disorders, or conditions associated with these tissues; and the vector into which each cDNA was cloned.

Table 4 describes the tissues used to construct the cDNA libraries from which cDNA clones encoding TRFX were isolated.

Table 5 shows the tools, programs, and algorithms used to analyze the polynucleotides and polypeptides of the invention, along with applicable descriptions, references, and threshold parameters.

DESCRIPTION OF THE INVENTION

Before the present proteins, nucleotide sequences, and methods are described, it is understood that this invention is not limited to the particular machines, materials and methods described, as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, a

reference to "a host cell" includes a plurality of such host cells, and a reference to "an antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any machines, materials, and methods similar or equivalent to those described herein can be used to practice or test the present invention, the preferred machines, materials and methods are now described. All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines, protocols, reagents and vectors which are reported in the publications and which might be used in connection with the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

DEFINITIONS

"TRFX" refers to the amino acid sequences of substantially purified TRFX obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and human, and from any source, whether natural, synthetic, semi-synthetic, or recombinant.

The term "agonist" refers to a molecule which intensifies or mimics the biological activity of TRFX. Agonists may include proteins, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of TRFX either by directly interacting with TRFX or by acting on components of the biological pathway in which TRFX participates.

An "allelic variant" is an alternative form of the gene encoding TRFX. Allelic variants may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. A gene may have none, one, or many allelic variants of its naturally occurring form. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

"Altered" nucleic acid sequences encoding TRFX include those sequences with deletions, insertions, or substitutions of different nucleotides, resulting in a polypeptide the same as TRFX or a polypeptide with at least one functional characteristic of TRFX. Included within this definition are polymorphisms which may or may not be readily detectable using a particular oligonucleotide probe of the polynucleotide encoding TRFX, and improper or unexpected hybridization to allelic variants, with a locus other than the normal chromosomal locus for the polynucleotide sequence encoding TRFX. The encoded protein may also be "altered," and may contain deletions, insertions, or substitutions of amino acid residues which produce a silent change and result in a functionally equivalent TRFX. Deliberate amino acid substitutions may be made on the basis of similarity in

polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the biological or immunological activity of TRFX is retained. For example, negatively charged amino acids may include aspartic acid and glutamic acid, and positively charged amino acids may include lysine and arginine. Amino acids with uncharged polar side chains having similar hydrophilicity values may include: asparagine and glutamine; and serine and threonine. Amino acids with uncharged side chains having similar hydrophilicity values may include: leucine, isoleucine, and valine; glycine and alanine; and phenylalanine and tyrosine.

The terms "amino acid" and "amino acid sequence" refer to an oligopeptide, peptide, polypeptide, or protein sequence, or a fragment of any of these, and to naturally occurring or synthetic molecules. Where "amino acid sequence" is recited to refer to a sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms are not meant to limit the amino acid sequence to the complete native amino acid sequence associated with the recited protein molecule.

"Amplification" relates to the production of additional copies of a nucleic acid sequence. Amplification is generally carried out using polymerase chain reaction (PCR) technologies well known in the art.

The term "antagonist" refers to a molecule which inhibits or attenuates the biological activity of TRFX. Antagonists may include proteins such as antibodies, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of TRFX either by directly interacting with TRFX or by acting on components of the biological pathway in which TRFX participates.

The term "antibody" refers to intact immunoglobulin molecules as well as to fragments thereof, such as Fab, $F(ab')_2$, and Fv fragments, which are capable of binding an epitopic determinant. Antibodies that bind TRFX polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the translation of RNA, or synthesized chemically, and can be conjugated to a carrier protein if desired. Commonly used carriers that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

The term "antigenic determinant" refers to that region of a molecule (i.e., an epitope) that makes contact with a particular antibody. When a protein or a fragment of a protein is used to immunize a host animal, numerous regions of the protein may induce the production of antibodies which bind specifically to antigenic determinants (particular regions or three-dimensional structures on the protein). An antigenic determinant may compete with the intact antigen (i.e., the immunogen used to elicit the immune response) for binding to an antibody.

The term "antisense" refers to any composition capable of base-pairing with the "sense" (coding) strand of a specific nucleic acid sequence. Antisense compositions may include DNA; RNA; peptide nucleic acid (PNA); oligonucleotides having modified backbone linkages such as phosphorothioates, methylphosphonates, or benzylphosphonates; oligonucleotides having modified sugar groups such as 2'-methoxyethyl sugars or 2'-methoxyethoxy sugars; or oligonucleotides having modified bases such as 5-methyl cytosine, 2'-deoxyuracil, or 7-deaza-2'-deoxyguanosine. Antisense molecules may be produced by any method including chemical synthesis or transcription. Once introduced into a cell, the complementary antisense molecule base-pairs with a naturally occurring nucleic acid sequence produced by the cell to form duplexes which block either transcription or translation. The designation "negative" or "minus" can refer to the antisense strand, and the designation "positive" or "plus" can refer to the sense strand of a reference DNA molecule.

The term "biologically active" refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule. Likewise, "immunologically active" or "immunogenic" refers to the capability of the natural, recombinant, or synthetic TRFX, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

"Complementary" describes the relationship between two single-stranded nucleic acid sequences that anneal by base-pairing. For example, 5'-AGT-3' pairs with its complement, 3'-TCA-5'.

A "composition comprising a given polynucleotide sequence" and a "composition comprising a given amino acid sequence" refer broadly to any composition containing the given polynucleotide or amino acid sequence. The composition may comprise a dry formulation or an aqueous solution. Compositions comprising polynucleotide sequences encoding TRFX or fragments of TRFX may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be associated with a stabilizing agent such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).

"Consensus sequence" refers to a nucleic acid sequence which has been subjected to repeated DNA sequence analysis to resolve uncalled bases, extended using the XL-PCR kit (Applied Biosystems, Foster City CA) in the 5' and/or the 3' direction, and resequenced, or which has been assembled from one or more overlapping cDNA, EST, or genomic DNA fragments using a computer program for fragment assembly, such as the GELVIEW fragment assembly system (GCG, Madison WI) or Phrap (University of Washington, Seattle WA). Some sequences have been both extended and assembled to produce the consensus sequence.

"Conservative amino acid substitutions" are those substitutions that are predicted to least

interfere with the properties of the original protein, i.e., the structure and especially the function of the protein is conserved and not significantly changed by such substitutions. The table below shows amino acids which may be substituted for an original amino acid in a protein and which are regarded as conservative amino acid substitutions.

Original Residue	Conservative Substitution
Ala	Gly, Ser
Arg	His, Lys
Asn	Asp, Gln, His
Asp	Asn, Glu
Cys	Ala, Ser
Gln	Asn, Glu, His
Glu	Asp, Gln, His
Gly	Ala
His	Asn, Arg, Gln, Glu
Ile	Leu, Val
Leu	Ile, Val
Lys	Arg, Gln, Glu
Met	Leu, Ile
Phe	His, Met, Leu, Trp, Tyr
Ser	Cys, Thr
Thr	Ser, Val
Trp	Phe, Tyr
Tyr	His, Phe, Trp
Val	Ile, Leu, Thr

Conservative amino acid substitutions generally maintain (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a beta sheet or alpha helical conformation, (b) the charge or hydrophobicity of the molecule at the site of the substitution, and/or (c) the bulk of the side chain.

A "deletion" refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

The term "derivative" refers to a chemically modified polynucleotide or polypeptide. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, hydroxyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

A "detectable label" refers to a reporter molecule or enzyme that is capable of generating a measurable signal and is covalently or noncovalently joined to a polynucleotide or polypeptide.

A "fragment" is a unique portion of TRFX or the polynucleotide encoding TRFX which is

identical in sequence to but shorter in length than the parent sequence. A fragment may comprise up to the entire length of the defined sequence, minus one nucleotide/amino acid residue. For example, a fragment may comprise from 5 to 1000 contiguous nucleotides or amino acid residues. A fragment used as a probe, primer, antigen, therapeutic molecule, or for other purposes, may be at least 5, 10, 15, 16, 20, 25, 30, 40, 50, 60, 75, 100, 150, 250 or at least 500 contiguous nucleotides or amino acid residues in length. Fragments may be preferentially selected from certain regions of a molecule. For example, a polypeptide fragment may comprise a certain length of contiguous amino acids selected from the first 250 or 500 amino acids (or first 25% or 50% of a polypeptide) as shown in a certain defined sequence. Clearly these lengths are exemplary, and any length that is supported by the specification, including the Sequence Listing, tables, and figures, may be encompassed by the present embodiments.

A fragment of SEQ ID NO:108-214 comprises a region of unique polynucleotide sequence that specifically identifies SEQ ID NO:108-214, for example, as distinct from any other sequence in the genome from which the fragment was obtained. A fragment of SEQ ID NO:108-214 is useful, for example, in hybridization and amplification technologies and in analogous methods that distinguish SEQ ID NO:108-214 from related polynucleotide sequences. The precise length of a fragment of SEQ ID NO:108-214 and the region of SEQ ID NO:108-214 to which the fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

A fragment of SEQ ID NO:1-107 is encoded by a fragment of SEQ ID NO:108-214. A fragment of SEQ ID NO:1-107 comprises a region of unique amino acid sequence that specifically identifies SEQ ID NO:1-107. For example, a fragment of SEQ ID NO:1-107 is useful as an immunogenic peptide for the development of antibodies that specifically recognize SEQ ID NO:1-107. The precise length of a fragment of SEQ ID NO:1-107 and the region of SEQ ID NO:1-107 to which the fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

A "full-length" polynucleotide sequence is one containing at least a translation initiation codon (e.g., methionine) followed by an open reading frame and a translation termination codon. A "full-length" polynucleotide sequence encodes a "full-length" polypeptide sequence.

"Homology" refers to sequence similarity or, interchangeably, sequence identity, between two or more polynucleotide sequences or two or more polypeptide sequences.

The terms "percent identity" and "% identity," as applied to polynucleotide sequences, refer to the percentage of residue matches between at least two polynucleotide sequences aligned using a standardized algorithm. Such an algorithm may insert, in a standardized and reproducible way, gaps in the sequences being compared in order to optimize alignment between two sequences, and

therefore achieve a more meaningful comparison of the two sequences.

Percent identity between polynucleotide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program. This program is part of the LASERGENE software package, a suite of molecular biological analysis programs (DNASTAR, Madison WI). CLUSTAL V is described in Higgins, D.G. and P.M. Sharp (1989) CABIOS 5:151-153 and in Higgins, D.G. et al. (1992) CABIOS 8:189-191. For pairwise alignments of polynucleotide sequences, the default parameters are set as follows: Ktuple=2, gap penalty=5, window=4, and "diagonals saved"=4. The "weighted" residue weight table is selected as the default. Percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polynucleotide sequences.

Alternatively, a suite of commonly used and freely available sequence comparison algorithms is provided by the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) (Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410), which is available from several sources, including the NCBI, Bethesda, MD, and on the Internet at http://www.ncbi.nlm.nih.gov/BLAST/. The BLAST software suite includes various sequence analysis programs including "blastn," that is used to align a known polynucleotide sequence with other polynucleotide sequences from a variety of databases. Also available is a tool called "BLAST 2 Sequences" that is used for direct pairwise comparison of two nucleotide sequences. "BLAST 2 Sequences" can be accessed and used interactively at http://www.ncbi.nlm.nih.gov/gorf/bl2.html. The "BLAST 2 Sequences" tool can be used for both blastn and blastp (discussed below). BLAST programs are commonly used with gap and other parameters set to default settings. For example, to compare two nucleotide sequences, one may use blastn with the "BLAST 2 Sequences" tool Version 2.0.12 (April-21-2000) set at default parameters. Such default parameters may be, for example:

Matrix: BLOSUM62

Reward for match: 1

Penalty for mismatch: -2

Open Gap: 5 and Extension Gap: 2 penalties

Gap x drop-off: 50

Expect: 10

Word Size: 11

Filter: on

Percent identity may be measured over the length of an entire defined sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined sequence, for instance, a fragment of at least 20, at least 30, at least 40, at least 50, at least 70, at least 100, or at least 200 contiguous

nucleotides. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures, or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

Nucleic acid sequences that do not show a high degree of identity may nevertheless encode similar amino acid sequences due to the degeneracy of the genetic code. It is understood that changes in a nucleic acid sequence can be made using this degeneracy to produce multiple nucleic acid sequences that all encode substantially the same protein.

The phrases "percent identity" and "% identity," as applied to polypeptide sequences, refer to the percentage of residue matches between at least two polypeptide sequences aligned using a standardized algorithm. Methods of polypeptide sequence alignment are well-known. Some alignment methods take into account conservative amino acid substitutions. Such conservative substitutions, explained in more detail above, generally preserve the charge and hydrophobicity at the site of substitution, thus preserving the structure (and therefore function) of the polypeptide.

Percent identity between polypeptide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program (described and referenced above). For pairwise alignments of polypeptide sequences using CLUSTAL V, the default parameters are set as follows: Ktuple=1, gap penalty=3, window=5, and "diagonals saved"=5. The PAM250 matrix is selected as the default residue weight table. As with polynucleotide alignments, the percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polypeptide sequence pairs.

Alternatively the NCBI BLAST software suite may be used. For example, for a pairwise comparison of two polypeptide sequences, one may use the "BLAST 2 Sequences" tool Version 2.0.12 (Apr-21-2000) with blastp set at default parameters. Such default parameters may be, for example:

Matrix: BLOSUM62

Open Gap: 11 and Extension Gap: 1 penalties

Gap x drop-off: 50

Expect: 10

Word Size: 3

Filter: on

Percent identity may be measured over the length of an entire defined polypeptide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polypeptide sequence, for instance, a fragment of at least 15, at least 20, at least 30, at least 40, at least 50, at least 70 or at least 150 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment

length supported by the sequences shown herein, in the tables, figures or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

"Human artificial chromosomes" (HACs) are linear microchromosomes which may contain DNA sequences of about 6 kb to 10 Mb in size, and which contain all of the elements required for chromosome replication, segregation and maintenance.

The term "humanized antibody" refers to an antibody molecule in which the amino acid sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

"Hybridization" refers to the process by which a polynucleotide strand anneals with a complementary strand through base pairing under defined hybridization conditions. Specific hybridization is an indication that two nucleic acid sequences share a high degree of complementarity. Specific hybridization complexes form under permissive annealing conditions and remain hybridized after the "washing" step(s). The washing step(s) is particularly important in determining the stringency of the hybridization process, with more stringent conditions allowing less non-specific binding, i.e., binding between pairs of nucleic acid strands that are not perfectly matched. Permissive conditions for annealing of nucleic acid sequences are routinely determinable by one of ordinary skill in the art and may be consistent among hybridization experiments, whereas wash conditions may be varied among experiments to achieve the desired stringency, and therefore hybridization specificity. Permissive annealing conditions occur, for example, at 68°C in the presence of about 6 x SSC, about 1% (w/v) SDS, and about 100 μg/ml sheared, denatured salmon sperm DNA.

Generally, stringency of hybridization is expressed, in part, with reference to the temperature under which the wash step is carried out. Such wash temperatures are typically selected to be about 5°C to 20°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength and pH) at which 50% of the target sequence hybridizes to a perfectly matched probe. An equation for calculating T_m and conditions for nucleic acid hybridization are well known and can be found in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; specifically see volume 2, chapter 9.

High stringency conditions for hybridization between polynucleotides of the present invention include wash conditions of 68°C in the presence of about 0.2 x SSC and about 0.1% SDS, for 1 hour. Alternatively, temperatures of about 65°C, 60°C, 55°C, or 42°C may be used. SSC concentration may be varied from about 0.1 to 2 x SSC, with SDS being present at about 0.1%. Typically, blocking reagents are used to block non-specific hybridization. Such blocking reagents include, for instance, sheared and denatured salmon sperm DNA at about 100-200 μg/ml. Organic solvent, such as formamide at a concentration of about 35-50% v/v, may also be used under particular

circumstances, such as for RNA:DNA hybridizations. Useful variations on these wash conditions will be readily apparent to those of ordinary skill in the art. Hybridization, particularly under high stringency conditions, may be suggestive of evolutionary similarity between the nucleotides. Such similarity is strongly indicative of a similar role for the nucleotides and their encoded polypeptides.

The term "hybridization complex" refers to a complex formed between two nucleic acid sequences by virtue of the formation of hydrogen bonds between complementary bases. A hybridization complex may be formed in solution (e.g., C_0t or R_0t analysis) or formed between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized on a solid support (e.g., paper, membranes, filters, chips, pins or glass slides, or any other appropriate substrate to which cells or their nucleic acids have been fixed).

The words "insertion" and "addition" refer to changes in an amino acid or nucleotide sequence resulting in the addition of one or more amino acid residues or nucleotides, respectively.

"Immune response" can refer to conditions associated with inflammation, trauma, immune disorders, or infectious or genetic disease, etc. These conditions can be characterized by expression of various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect cellular and systemic defense systems.

An "immunogenic fragment" is a polypeptide or oligopeptide fragment of TRFX which is capable of eliciting an immune response when introduced into a living organism, for example, a mammal. The term "immunogenic fragment" also includes any polypeptide or oligopeptide fragment of TRFX which is useful in any of the antibody production methods disclosed herein or known in the art.

The term "microarray" refers to an arrangement of a plurality of polynucleotides, polypeptides, or other chemical compounds on a substrate.

The terms "element" and "array element" refer to a polynucleotide, polypeptide, or other chemical compound having a unique and defined position on a microarray.

The term "modulate" refers to a change in the activity of TRFX. For example, modulation may cause an increase or a decrease in protein activity, binding characteristics, or any other biological, functional, or immunological properties of TRFX.

The phrases "nucleic acid" and "nucleic acid sequence" refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material.

"Operably linked" refers to the situation in which a first nucleic acid sequence is placed in a functional relationship with a second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding

sequence. Operably linked DNA sequences may be in close proximity or contiguous and, where necessary to join two protein coding regions, in the same reading frame.

"Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers solubility to the composition. PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation, and may be pegylated to extend their lifespan in the cell.

"Post-translational modification" of an TRFX may involve lipidation, glycosylation, phosphorylation, acetylation, racemization, proteolytic cleavage, and other modifications known in the art. These processes may occur synthetically or biochemically. Biochemical modifications will vary by cell type depending on the enzymatic milieu of TRFX.

"Probe" refers to nucleic acid sequences encoding TRFX, their complements, or fragments thereof, which are used to detect identical, allelic or related nucleic acid sequences. Probes are isolated oligonucleotides or polynucleotides attached to a detectable label or reporter molecule. Typical labels include radioactive isotopes, ligands, chemiluminescent agents, and enzymes. "Primers" are short nucleic acids, usually DNA oligonucleotides, which may be annealed to a target polynucleotide by complementary base-pairing. The primer may then be extended along the target DNA strand by a DNA polymerase enzyme. Primer pairs can be used for amplification (and identification) of a nucleic acid sequence, e.g., by the polymerase chain reaction (PCR).

Probes and primers as used in the present invention typically comprise at least 15 contiguous nucleotides of a known sequence. In order to enhance specificity, longer probes and primers may also be employed, such as probes and primers that comprise at least 20, 25, 30, 40, 50, 60, 70, 80, 90, 100, or at least 150 consecutive nucleotides of the disclosed nucleic acid sequences. Probes and primers may be considerably longer than these examples, and it is understood that any length supported by the specification, including the tables, figures, and Sequence Listing, may be used.

Methods for preparing and using probes and primers are described in the references, for example Sambrook, J. et al. (1989) Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; Ausubel, F.M. et al. (1987) Current Protocols in Molecular Biology, Greene Publ. Assoc. & Wiley-Intersciences, New York NY; Innis, M. et al. (1990) PCR Protocols, A Guide to Methods and Applications, Academic Press, San Diego CA. PCR primer pairs can be derived from a known sequence, for example, by using computer programs intended for that purpose such as Primer (Version 0.5, 1991, Whitehead Institute for Biomedical Research, Cambridge MA).

Oligonucleotides for use as primers are selected using software known in the art for such purpose. For example, OLIGO 4.06 software is useful for the selection of PCR primer pairs of up to

100 nucleotides each, and for the analysis of oligonucleotides and larger polynucleotides of up to 5,000 nucleotides from an input polynucleotide sequence of up to 32 kilobases. Similar primer selection programs have incorporated additional features for expanded capabilities. For example, the PrimOU primer selection program (available to the public from the Genome Center at University of Texas South West Medical Center, Dallas TX) is capable of choosing specific primers from megabase sequences and is thus useful for designing primers on a genome-wide scope. The Primer3 primer selection program (available to the public from the Whitehead Institute/MIT Center for Genome Research, Cambridge MA) allows the user to input a "mispriming library," in which sequences to avoid as primer binding sites are user-specified. Primer3 is useful, in particular, for the selection of oligonucleotides for microarrays. (The source code for the latter two primer selection programs may also be obtained from their respective sources and modified to meet the user's specific needs.) The PrimeGen program (available to the public from the UK Human Genome Mapping Project Resource Centre, Cambridge UK) designs primers based on multiple sequence alignments, thereby allowing selection of primers that hybridize to either the most conserved or least conserved regions of aligned nucleic acid sequences. Hence, this program is useful for identification of both unique and conserved oligonucleotides and polynucleotide fragments. The oligonucleotides and polynucleotide fragments identified by any of the above selection methods are useful in hybridization technologies, for example, as PCR or sequencing primers, microarray elements, or specific probes to identify fully or partially complementary polynucleotides in a sample of nucleic acids. Methods of oligonucleotide selection are not limited to those described above.

A "recombinant nucleic acid" is a sequence that is not naturally occurring or has a sequence that is made by an artificial combination of two or more otherwise separated segments of sequence. This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, e.g., by genetic engineering techniques such as those described in Sambrook, supra. The term recombinant includes nucleic acids that have been altered solely by addition, substitution, or deletion of a portion of the nucleic acid. Frequently, a recombinant nucleic acid may include a nucleic acid sequence operably linked to a promoter sequence. Such a recombinant nucleic acid may be part of a vector that is used, for example, to transform a cell.

Alternatively, such recombinant nucleic acids may be part of a viral vector, e.g., based on a vaccinia virus, that could be use to vaccinate a mammal wherein the recombinant nucleic acid is expressed, inducing a protective immunological response in the mammal.

A "regulatory element" refers to a nucleic acid sequence usually derived from untranslated regions of a gene and includes enhancers, promoters, introns, and 5' and 3' untranslated regions (UTRs). Regulatory elements interact with host or viral proteins which control transcription,

translation, or RNA stability.

"Reporter molecules" are chemical or biochemical moieties used for labeling a nucleic acid, amino acid, or antibody. Reporter molecules include radionuclides; enzymes; fluorescent, chemiluminescent, or chromogenic agents; substrates; cofactors; inhibitors; magnetic particles; and other moieties known in the art.

An "RNA equivalent," in reference to a DNA sequence, is composed of the same linear sequence of nucleotides as the reference DNA sequence with the exception that all occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

The term "sample" is used in its broadest sense. A sample suspected of containing nucleic acids encoding TRFX, or fragments thereof, or TRFX itself, may comprise a bodily fluid; an extract from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

The terms "specific binding" and "specifically binding" refer to that interaction between a protein or peptide and an agonist, an antibody, an antagonist, a small molecule, or any natural or synthetic binding composition. The interaction is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the presence of a polypeptide comprising the epitope A, or the presence of free unlabeled A, in a reaction containing free labeled A and the antibody will reduce the amount of labeled A that binds to the antibody.

The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least 60% free, preferably at least 75% free, and most preferably at least 90% free from other components with which they are naturally associated.

A "substitution" refers to the replacement of one or more amino acid residues or nucleotides by different amino acid residues or nucleotides, respectively.

"Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

A "transcript image" refers to the collective pattern of gene expression by a particular cell type or tissue under given conditions at a given time.

"Transformation" describes a process by which exogenous DNA is introduced into a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid

sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected based on the type of host cell being transformed and may include, but is not limited to, bacteriophage or viral infection, electroporation, heat shock, lipofection, and particle bombardment. The term "transformed" cells includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "transgenic organism," as used herein, is any organism, including but not limited to animals and plants, in which one or more of the cells of the organism contains heterologous nucleic acid introduced by way of human intervention, such as by transgenic techniques well known in the art. The nucleic acid is introduced into the cell, directly or indirectly by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by microinjection or by infection with a recombinant virus. The term genetic manipulation does not include classical cross-breeding, or in vitro fertilization, but rather is directed to the introduction of a recombinant DNA molecule. The transgenic organisms contemplated in accordance with the present invention include bacteria, cyanobacteria, fungi, plants, and animals. The isolated DNA of the present invention can be introduced into the host by methods known in the art, for example infection, transfection, transformation or transconjugation. Techniques for transferring the DNA of the present invention into such organisms are widely known and provided in references such as Sambrook, J. et al. (1989), supra.

A "variant" of a particular nucleic acid sequence is defined as a nucleic acid sequence having at least 40% sequence identity to the particular nucleic acid sequence over a certain length of one of the nucleic acid sequences using blastn with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of nucleic acids may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95% or at least 98% or greater sequence identity over a certain defined length. A variant may be described as, for example, an "allelic" (as defined above), "splice," "species," or "polymorphic" variant. A splice variant may have significant identity to a reference molecule, but will generally have a greater or lesser number of polynucleotides due to alternative splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or lack domains that are present in the reference molecule. Species variants are polynucleotide sequences that vary from one species to another. The resulting polypeptides generally will have significant amino acid identity relative to each other. A polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass "single nucleotide polymorphisms" (SNPs) in which the polynucleotide sequence varies by one nucleotide base. The presence of SNPs may be indicative of, for example, a certain population, a disease state, or a

propensity for a disease state.

A "variant" of a particular polypeptide sequence is defined as a polypeptide sequence having at least 40% sequence identity to the particular polypeptide sequence over a certain length of one of the polypeptide sequences using blastp with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of polypeptides may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or at least 98% or greater sequence identity over a certain defined length of one of the polypeptides.

THE INVENTION

The invention is based on the discovery of new human transcription factors (TRFX), the polynucleotides encoding TRFX, and the use of these compositions for the diagnosis, treatment, or prevention of cell proliferative, autoimmune/inflammatory, neurological, and developmental disorders.

Table 1 lists the Incyte clones used to assemble full length nucleotide sequences encoding TRFX. Columns 1 and 2 show the sequence identification numbers (SEQ ID NOs) of the polypeptide and nucleotide sequences, respectively. Column 3 shows the clone IDs of the Incyte clones in which nucleic acids encoding each TRFX were identified, and column 4 shows the cDNA libraries from which these clones were isolated. Column 5 shows Incyte clones and their corresponding cDNA libraries. Clones for which cDNA libraries are not indicated were derived from pooled cDNA libraries. In some cases, GenBank sequence identifiers are also shown in column 5. The Incyte clones and GenBank cDNA sequences, where indicated, in column 5 were used to assemble the consensus nucleotide sequence of each TRFX and are useful as fragments in hybridization technologies.

The columns of Table 2 show various properties of each of the polypeptides of the invention: column 1 references the SEQ ID NO and Incyte clone ID of each polypeptide; column 2 shows the number of amino acid residues in each polypeptide; column 3 shows potential phosphorylation sites; column 4 shows potential glycosylation sites; column 5 shows the amino acid residues comprising signature sequences and motifs; column 6 shows homologous sequences as identified by BLAST analysis along with relevant citations, all of which are expressly incorporated by reference herein in their entirety; and column 7 shows analytical methods and in some cases, searchable databases to which the analytical methods were applied. The methods of column 7 were used to characterize each polypeptide through sequence homology and protein motifs.

The columns of Table 3 show the tissue-specificity and diseases, disorders, or conditions associated with nucleotide sequences encoding TRFX. The first column of Table 3 lists the nucleotide SEQ ID NOs and Incyte Clone IDs. Fragments of these polynucleotides are useful, for example, in hybridization or amplification technologies to identify SEQ ID NO:108-214 and to distinguish between SEQ ID NO:108-214 and related polynucleotide sequences. The polypeptides

encoded by these fragments are useful, for example, as immunogenic peptides. Column 2 lists tissue categories which express TRFX as a fraction of total tissues expressing TRFX. Column 3 lists diseases, disorders, or conditions associated with those tissues expressing TRFX as a fraction of total tissues expressing TRFX. Column 4 lists the vectors used to subclone each cDNA library.

The columns of Table 4 show descriptions of the tissues used to construct the cDNA libraries from which cDNA clones encoding TRFX were isolated. Column 1 references the nucleotide SEQ ID NOs and Incyte Clone IDs, column 2 shows the cDNA libraries from which these clones were isolated, and column 3 shows the tissue origins and other descriptive information relevant to the cDNA libraries in column 2.

SEQ ID NO:111 maps to chromosome 6 within the interval from 89.4 to 96.1 centiMorgans.

SEQ ID NO:114 maps to chromosome 6 within the interval from 42.0 to 44.9 centiMorgans.

SEQ ID NO:117 maps to chromosome 13 within the interval from 95.9 to 112.7 centiMorgans.

SEQ ID NO:122 maps to chromosome 3 within the interval from 55.4 to 63.3 centiMorgans.

SEQ ID NO:123 maps to chromosome 7 within the interval from 149.6 to 159.0 centiMorgans.

SEQ ID NO:125 maps to chromosome 15 within the interval from 45.5 to 58.8 centiMorgans.

SEQ ID NO:130 maps to chromosome 1 within the interval from 152.2 to 156.1 centiMorgans.

SEQ ID NO:132 maps to chromosome 1 within the interval from 36.2 to 54.2 centiMorgans.

SEQ ID NO:133 maps to chromosome 19 within the interval from 41.7 to 49.4 centiMorgans.

SEQ ID NO:134 maps to chromosome 17 within the interval from 99.3 to 104.7 centiMorgans.

SEQ ID NO:136 maps to chromosome 16 within the interval from 119.2 centiMorgans to the q-terminus.

SEQ ID NO:138 maps to chromosome 19 within the interval from 60.9 to 61.4 centiMorgans.

SEQ ID NO:145 maps to chromosome 2 within the interval from 190.8 to 196.8 centiMorgans and to chromosome 10 within the interval from 68.7 to 72.5 centiMorgans.

SEQ ID NO:149 maps to chromosome 3 within the interval from the p terminus to 16.5 centiMorgans.

SEQ ID NO:152 maps to chromosome 19 within the interval from 35.5 to 49.4 centiMorgans and to chromosome 7 within the interval from 100.5 to 114.5 centiMorgans and to chromosome 7 within the intervals from 67.6 to 69.3 centiMorgans and 83.8 centiMorgans and the q-terminus.

SEQ ID NO:153 maps to chromosome 16 within the interval from 65.6 to 72.6 centiMorgans.

SEQ ID NO:156 maps to chromosome 20 within the interval from 65.5 to 79.0 centiMorgans.

SEQ ID NO:159 maps to chromosome 18 within the interval from 40.4 to 49.7 centiMorgans.

SEQ ID NO:168 maps to chromosome 23 within the interval from 112.8 to 139.4 centiMorgans.

SEQ ID NO:179 maps to chromosome 11 within the interval from 16.7 to 24.7 centiMorgans.

SEQ ID NO:180 maps to chromosome 16 within the interval from 33.3 to 42.7 centiMorgans

SEQ ID NO:184 maps to chromosome 2 within the interval from 190.5 to 196.8 centiMorgans and within the interval from the p terminus to 16.4 centiMorgans.

SEQ ID NO:185 maps to chromosome 9 within the interval from 20.4 to 27.8 centiMorgans and from the p terminus to 33.3 centiMorgans.

SEQ ID NO:196 maps to chromosome 1 within the interval from 57.2 to 57.5 centiMorgans.

SEQ ID NO:197 maps to chromosome 19 within the interval from 60.9 to 61.4 centiMorgans.

SEQ ID NO:199 maps to chromosome 13 within the interval from 77.1 to 86.9 centiMorgans and to chromosome 2 within the interval from 51.2 to 51.8 centiMorgans.

SEQ ID NO:201 maps to chromosome 22 within the interval from 22.2 to 40.2 centiMorgans.

SEQ ID NO:204 maps to chromosome 5 within the interval from 132.8 to 141.4 centiMorgans.

SEQ ID NO:208 maps to chromosome 13 within the interval from 37.3 to 45.8 centiMorgans and to chromosome 19 within the interval from 58.1 to 58.7 centiMorgans.

SEQ ID NO:212 maps to chromosome 19 within the interval from the p terminus to 35.5 centiMorgans and to chromosome 20 within the interval from 50.2 to 53.6.

SEQ ID NO:213 maps to chromosome 6 within the interval from the p terminus to 14.2 centiMorgans.

The invention also encompasses TRFX variants. A preferred TRFX variant is one which has at least about 80%, or alternatively at least about 90%, or even at least about 95% amino acid sequence identity to the TRFX amino acid sequence, and which contains at least one functional or structural characteristic of TRFX.

The invention also encompasses polynucleotides which encode TRFX. In a particular embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:108-214, which encodes TRFX. The polynucleotide sequences of SEQ ID NO:108-214, as presented in the Sequence Listing, embrace the equivalent RNA sequences, wherein occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

The invention also encompasses a variant of a polynucleotide sequence encoding TRFX. In particular, such a variant polynucleotide sequence will have at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to the polynucleotide

sequence encoding TRFX. A particular aspect of the invention encompasses a variant of a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:108-214 which has at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:108-214. Any one of the polynucleotide variants described above can encode an amino acid sequence which contains at least one functional or structural characteristic of TRFX.

It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding TRFX, some bearing minimal similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet genetic code as applied to the polynucleotide sequence of naturally occurring TRFX, and all such variations are to be considered as being specifically disclosed.

Although nucleotide sequences which encode TRFX and its variants are generally capable of hybridizing to the nucleotide sequence of the naturally occurring TRFX under appropriately selected conditions of stringency, it may be advantageous to produce nucleotide sequences encoding TRFX or its derivatives possessing a substantially different codon usage, e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding TRFX and its derivatives without altering the encoded amino acid sequences include the production of RNA transcripts having more desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of DNA sequences which encode TRFX and TRFX derivatives, or fragments thereof, entirely by synthetic chemistry. After production, the synthetic sequence may be inserted into any of the many available expression vectors and cell systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce mutations into a sequence encoding TRFX or any fragment thereof.

Also encompassed by the invention are polynucleotide sequences that are capable of hybridizing to the claimed polynucleotide sequences, and, in particular, to those shown in SEQ ID NO:108-214 and fragments thereof under various conditions of stringency. (See, e.g., Wahl, G.M. and S.L. Berger (1987) Methods Enzymol. 152:399-407; Kimmel, A.R. (1987) Methods Enzymol. 152:507-511.) Hybridization conditions, including annealing and wash conditions, are described in "Definitions."

Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (Applied Biosystems, Foster City CA), thermostable T7 polymerase (Amersham Pharmacia Biotech, Piscataway NJ), or combinations of polymerases and proofreading exonucleases such as those found in the ELONGASE amplification system (Life Technologies, Gaithersburg MD). Preferably, sequence preparation is automated with machines such as the MICROLAB 2200 liquid transfer system (Hamilton, Reno NV), PTC200 thermal cycler (MJ Research, Watertown MA) and ABI CATALYST 800 thermal cycler (Applied Biosystems). Sequencing is then carried out using either the ABI 373 or 377 DNA sequencing system (Applied Biosystems), the MEGABACE 1000 DNA sequencing system (Molecular Dynamics, Sunnyvale CA), or other systems known in the art. The resulting sequences are analyzed using a variety of algorithms which are well known in the art. (See, e.g., Ausubel, F.M. (1997) Short Protocols in Molecular Biology, John Wiley & Sons, New York NY, unit 7.7; Meyers, R.A. (1995) Molecular Biology and Biotechnology, Wiley VCH, New York NY, pp. 856-853.)

The nucleic acid sequences encoding TRFX may be extended utilizing a partial nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences, such as promoters and regulatory elements. For example, one method which may be employed, restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic DNA within a cloning vector. (See, e.g., Sarkar, G. (1993) PCR Methods Applic. 2:318-322.) Another method, inverse PCR, uses primers that extend in divergent directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a known genomic locus and surrounding sequences. (See, e.g., Triglia, T. et al. (1988) Nucleic Acids Res. 16:8186.) A third method, capture PCR, involves PCR amplification of DNA fragments adjacent to known sequences in human and yeast artificial chromosome DNA. (See, e.g., Lagerstrom, M. et al. (1991) PCR Methods Applic. 1:111-119.) In this method, multiple restriction enzyme digestions and ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences are known in the art. (See, e.g., Parker, J.D. et al. (1991) Nucleic Acids Res. 19:3055-3060). Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic DNA. This procedure avoids the need to screen libraries and is useful in finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences, Plymouth MN) or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the template at temperatures of

about 68°C to 72°C.

When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.

Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic separation, four different nucleotide-specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the emitted wavelengths. Output/light intensity may be converted to electrical signal using appropriate software (e.g., GENOTYPER and SEQUENCE NAVIGATOR, Applied Biosystems), and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments which may be present in limited amounts in a particular sample.

In another embodiment of the invention, polynucleotide sequences or fragments thereof which encode TRFX may be cloned in recombinant DNA molecules that direct expression of TRFX, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be produced and used to express TRFX.

The nucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter TRFX-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

The nucleotides of the present invention may be subjected to DNA shuffling techniques such as MOLECULARBREEDING (Maxygen Inc., Santa Clara CA; described in U.S. Patent Number 5,837,458; Chang, C.-C. et al. (1999) Nat. Biotechnol. 17:793-797; Christians, F.C. et al. (1999) Nat. Biotechnol. 17:259-264; and Crameri, A. et al. (1996) Nat. Biotechnol. 14:315-319) to alter or improve the biological properties of TRFX, such as its biological or enzymatic activity or its ability to bind to other molecules or compounds. DNA shuffling is a process by which a library of gene variants is produced using PCR-mediated recombination of gene fragments. The library is then subjected to selection or screening procedures that identify those gene variants with the desired

properties. These preferred variants may then be pooled and further subjected to recursive rounds of DNA shuffling and selection/screening. Thus, genetic diversity is created through "artificial" breeding and rapid molecular evolution. For example, fragments of a single gene containing random point mutations may be recombined, screened, and then reshuffled until the desired properties are optimized. Alternatively, fragments of a given gene may be recombined with fragments of homologous genes in the same gene family, either from the same or different species, thereby maximizing the genetic diversity of multiple naturally occurring genes in a directed and controllable manner.

In another embodiment, sequences encoding TRFX may be synthesized, in whole or in part, using chemical methods well known in the art. (See, e.g., Caruthers, M.H. et al. (1980) Nucleic Acids Symp. Ser. 7:215-223; Horn, T. et al. (1980) Nucleic Acids Symp. Ser. 7:225-232.) Alternatively, TRFX itself or a fragment thereof may be synthesized using chemical methods. For example, peptide synthesis can be performed using various solution-phase or solid-phase techniques. (See, e.g., Creighton, T. (1984) Proteins, Structures and Molecular Properties, WH Freeman, New York NY, pp. 55-60; and Roberge, J.Y. et al. (1995) Science 269:202-204.) Automated synthesis may be achieved using the ABI 431A peptide synthesizer (Applied Biosystems). Additionally, the amino acid sequence of TRFX, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide or a polypeptide having a sequence of a naturally occurring polypeptide.

The peptide may be substantially purified by preparative high performance liquid chromatography. (See, e.g., Chiez, R.M. and F.Z. Regnier (1990) Methods Enzymol. 182:392-421.) The composition of the synthetic peptides may be confirmed by amino acid analysis or by sequencing. (See, e.g., Creighton, supra, pp. 28-53.)

In order to express a biologically active TRFX, the nucleotide sequences encoding TRFX or derivatives thereof may be inserted into an appropriate expression vector, i.e., a vector which contains the necessary elements for transcriptional and translational control of the inserted coding sequence in a suitable host. These elements include regulatory sequences, such as enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotide sequences encoding TRFX. Such elements may vary in their strength and specificity. Specific initiation signals may also be used to achieve more efficient translation of sequences encoding TRFX. Such signals include the ATG initiation codon and adjacent sequences, e.g. the Kozak sequence. In cases where sequences encoding TRFX and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous translational control signals including an in-frame ATG initiation codon should be

provided by the vector. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used. (See, e.g., Scharf, D. et al. (1994) Results Probl. Cell Differ. 20:125-162.)

Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding TRFX and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. (See, e.g., Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel, F.M. et al. (1995) Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, ch. 9, 13, and 16.)

A variety of expression vector/host systems may be utilized to contain and express sequences encoding TRFX. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with viral expression vectors (e.g., baculovirus); plant cell systems transformed with viral expression vectors (e.g., cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems. (See, e.g., Sambrook, supra; Ausubel, supra; Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509; Bitter, G.A. et al. (1987) Methods Enzymol. 153:516-544; Scorer, C.A. et al. (1994) Bio/Technology 12:181-184; Engelhard, E.K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945; Takamatsu, N. (1987) EMBO J. 6:307-311; Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al. (1984) Science 224:838-843; Winter, J. et al. (1991) Results Probl. Cell Differ. 17:85-105; The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196; Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. USA 81:3655-3659; and Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355.) Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids, may be used for delivery of nucleotide sequences to the targeted organ, tissue, or cell population. (See, e.g., Di Nicola, M. et al. (1998) Cancer Gen. Ther. 5(6):350-356; Yu, M. et al. (1993) Proc. Natl. Acad. Sci. USA 90(13):6340-6344; Buller, R.M. et al. (1985) Nature 317(6040):813-815; McGregor, D.P. et al. (1994) Mol. Immunol. 31(3):219-226; and Verma, I.M. and N. Somia (1997) Nature 389:239-242.) The invention is not limited by the host cell employed.

In bacterial systems, a number of cloning and expression vectors may be selected depending upon the use intended for polynucleotide sequences encoding TRFX. For example, routine cloning, subcloning, and propagation of polynucleotide sequences encoding TRFX can be achieved using a

multifunctional E. coli vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or PSPORT1 plasmid (Life Technologies). Ligation of sequences encoding TRFX into the vector's multiple cloning site disrupts the *lacZ* gene, allowing a colorimetric screening procedure for identification of transformed bacteria containing recombinant molecules. In addition, these vectors may be useful for in vitro transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of nested deletions in the cloned sequence. (See, e.g., Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509.) When large quantities of TRFX are needed, e.g. for the production of antibodies, vectors which direct high level expression of TRFX may be used. For example, vectors containing the strong, inducible T5 or T7 bacteriophage promoter may be used.

Yeast expression systems may be used for production of TRFX. A number of vectors containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH promoters, may be used in the yeast Saccharomyces cerevisiae or Pichia pastoris. In addition, such vectors direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign sequences into the host genome for stable propagation. (See, e.g., Ausubel, 1995, supra; Bitter, supra; and Scorer, supra.)

Plant systems may also be used for expression of TRFX. Transcription of sequences encoding TRFX may be driven viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J. 6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used. (See, e.g., Coruzzi, supra; Broglie, supra; and Winter, supra.) These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. (See, e.g., The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196.)

In mammalian cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, sequences encoding TRFX may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses TRFX in host cells. (See, e.g., Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. USA 81:3655-3659.) In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells. SV40 or EBV-based vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are constructed and delivered via conventional delivery methods (liposomes, polycationic amino polymers, or vesicles) for therapeutic purposes. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet.

15:345-355.)

For long term production of recombinant proteins in mammalian systems, stable expression of TRFX in cell lines is preferred. For example, sequences encoding TRFX can be transformed into cell lines using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in *tk*⁻ and *apr*⁻ cells, respectively. (See, e.g., Wigler, M. et al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823.) Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, *dhfr* confers resistance to methotrexate; *neo* confers resistance to the aminoglycosides neomycin and G-418; and *als* and *pat* confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. (See, e.g., Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. USA 77:3567-3570; Colbere-Garapin, F. et al. (1981) J. Mol. Biol. 150:1-14.) Additional selectable genes have been described, e.g., *trpB* and *hisD*, which alter cellular requirements for metabolites. (See, e.g., Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. USA 85:8047-8051.) Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP; Clontech), ß glucuronidase and its substrate ß-glucuronide, or luciferase and its substrate luciferin may be used. These markers can be used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system. (See, e.g., Rhodes, C.A. (1995) Methods Mol. Biol. 55:121-131.)

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the sequence encoding TRFX is inserted within a marker gene sequence, transformed cells containing sequences encoding TRFX can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a sequence encoding TRFX under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

In general, host cells that contain the nucleic acid sequence encoding TRFX and that express TRFX may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR

amplification, and protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein sequences.

Immunological methods for detecting and measuring the expression of TRFX using either specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on TRFX is preferred, but a competitive binding assay may be employed. These and other assays are well known in the art. (See, e.g., Hampton, R. et al. (1990) Serological Methods, a Laboratory Manual, APS Press, St. Paul MN, Sect. IV; Coligan, J.E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New York NY; and Pound, J.D. (1998) Immunochemical Protocols, Humana Press, Totowa NJ.)

A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding TRFX include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, the sequences encoding TRFX, or any fragments thereof, may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Pharmacia Biotech, Promega (Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be used for ease of detection include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with nucleotide sequences encoding TRFX may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode TRFX may be designed to contain signal sequences which direct secretion of TRFX through a prokaryotic or eukaryotic cell membrane.

In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" or "pro" form of the protein may also be used to specify protein targeting, folding, and/or activity.

Different host cells which have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and WI38) are available from the American Type Culture Collection (ATCC, Manassas VA) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences encoding TRFX may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric TRFX protein containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of TRFX activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG, *c-myc*, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, *c-myc*, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be engineered to contain a proteolytic cleavage site located between the TRFX encoding sequence and the heterologous protein sequence, so that TRFX may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch. 10). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

In a further embodiment of the invention, synthesis of radiolabeled TRFX may be achieved in vitro using the TNT rabbit reticulocyte lysate or wheat germ extract system (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, for example, ^{35}S-methionine.

TRFX of the present invention or fragments thereof may be used to screen for compounds that specifically bind to TRFX. At least one and up to a plurality of test compounds may be screened for specific binding to TRFX. Examples of test compounds include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

In one embodiment, the compound thus identified is closely related to the natural ligand of TRFX, e.g., a ligand or fragment thereof, a natural substrate, a structural or functional mimetic, or a natural binding partner. (See, e.g., Coligan, J.E. et al. (1991) Current Protocols in Immunology 1(2): Chapter 5.) Similarly, the compound can be closely related to the natural receptor to which TRFX

binds, or to at least a fragment of the receptor, e.g., the ligand binding site. In either case, the compound can be rationally designed using known techniques. In one embodiment, screening for these compounds involves producing appropriate cells which express TRFX, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, Drosophila, or E. coli. Cells expressing TRFX or cell membrane fractions which contain TRFX are then contacted with a test compound and binding, stimulation, or inhibition of activity of either TRFX or the compound is analyzed.

An assay may simply test binding of a test compound to the polypeptide, wherein binding is detected by a fluorophore, radioisotope, enzyme conjugate, or other detectable label. For example, the assay may comprise the steps of combining at least one test compound with TRFX, either in solution or affixed to a solid support, and detecting the binding of TRFX to the compound. Alternatively, the assay may detect or measure binding of a test compound in the presence of a labeled competitor. Additionally, the assay may be carried out using cell-free preparations, chemical libraries, or natural product mixtures, and the test compound(s) may be free in solution or affixed to a solid support.

TRFX of the present invention or fragments thereof may be used to screen for compounds that modulate the activity of TRFX. Such compounds may include agonists, antagonists, or partial or inverse agonists. In one embodiment, an assay is performed under conditions permissive for TRFX activity, wherein TRFX is combined with at least one test compound, and the activity of TRFX in the presence of a test compound is compared with the activity of TRFX in the absence of the test compound. A change in the activity of TRFX in the presence of the test compound is indicative of a compound that modulates the activity of TRFX. Alternatively, a test compound is combined with an in vitro or cell-free system comprising TRFX under conditions suitable for TRFX activity, and the assay is performed. In either of these assays, a test compound which modulates the activity of TRFX may do so indirectly and need not come in direct contact with the test compound. At least one and up to a plurality of test compounds may be screened.

In another embodiment, polynucleotides encoding TRFX or their mammalian homologs may be "knocked out" in an animal model system using homologous recombination in embryonic stem (ES) cells. Such techniques are well known in the art and are useful for the generation of animal models of human disease. (See, e.g., U.S. Patent No. 5,175,383 and U.S. Patent No. 5,767,337.) For example, mouse ES cells, such as the mouse 129/SvJ cell line, are derived from the early mouse embryo and grown in culture. The ES cells are transformed with a vector containing the gene of interest disrupted by a marker gene, e.g., the neomycin phosphotransferase gene (neo; Capecchi, M.R. (1989) Science 244:1288-1292). The vector integrates into the corresponding region of the host

genome by homologous recombination. Alternatively, homologous recombination takes place using the Cre-loxP system to knockout a gene of interest in a tissue- or developmental stage-specific manner (Marth, J.D. (1996) Clin. Invest. 97:1999-2002; Wagner, K.U. et al. (1997) Nucleic Acids Res. 25:4323-4330). Transformed ES cells are identified and microinjected into mouse cell blastocysts such as those from the C57BL/6 mouse strain. The blastocysts are surgically transferred to pseudopregnant dams, and the resulting chimeric progeny are genotyped and bred to produce heterozygous or homozygous strains. Transgenic animals thus generated may be tested with potential therapeutic or toxic agents.

Polynucleotides encoding TRFX may also be manipulated in vitro in ES cells derived from human blastocysts. Human ES cells have the potential to differentiate into at least eight separate cell lineages including endoderm, mesoderm, and ectodermal cell types. These cell lineages differentiate into, for example, neural cells, hematopoietic lineages, and cardiomyocytes (Thomson, J.A. et al. (1998) Science 282:1145-1147).

Polynucleotides encoding TRFX can also be used to create "knockin" humanized animals (pigs) or transgenic animals (mice or rats) to model human disease. With knockin technology, a region of a polynucleotide encoding TRFX is injected into animal ES cells, and the injected sequence integrates into the animal cell genome. Transformed cells are injected into blastulae, and the blastulae are implanted as described above. Transgenic progeny or inbred lines are studied and treated with potential pharmaceutical agents to obtain information on treatment of a human disease. Alternatively, a mammal inbred to overexpress TRFX, e.g., by secreting TRFX in its milk, may also serve as a convenient source of that protein (Janne, J. et al. (1998) Biotechnol. Annu. Rev. 4:55-74).

THERAPEUTICS

Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of TRFX and transcription factors. In addition, the expression of TRFX is closely associated with reproductive, nervous, and hematopoeitic/immune tissues. Therefore, TRFX appears to play a role in cell proliferative, autoimmune/inflammatory, neurological, and developmental disorders. In the treatment of disorders associated with increased TRFX expression or activity, it is desirable to decrease the expression or activity of TRFX. In the treatment of disorders associated with decreased TRFX expression or activity, it is desirable to increase the expression or activity of TRFX.

Therefore, in one embodiment, TRFX or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of TRFX. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed

connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; an autoimmune/inflammatory disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; a neurological disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system including Down syndrome, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, seasonal affective disorder (SAD),

akathesia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, Tourette's disorder, progressive supranuclear palsy, corticobasal degeneration, and familial frontotemporal dementia; and a developmental disorder such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy, gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and mental retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratodermas, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Syndenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract, and sensorineural hearing loss.

In another embodiment, a vector capable of expressing TRFX or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of TRFX including, but not limited to, those described above.

In a further embodiment, a composition comprising a substantially purified TRFX in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of TRFX including, but not limited to, those provided above.

In still another embodiment, an agonist which modulates the activity of TRFX may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of TRFX including, but not limited to, those listed above.

In a further embodiment, an antagonist of TRFX may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of TRFX. Examples of such disorders include, but are not limited to, those cell proliferative, autoimmune/inflammatory, neurological, and developmental disorders described above. In one aspect, an antibody which specifically binds TRFX may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissues which express TRFX.

In an additional embodiment, a vector expressing the complement of the polynucleotide encoding TRFX may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of TRFX including, but not limited to, those described above.

In other embodiments, any of the proteins, antagonists, antibodies, agonists, complementary sequences, or vectors of the invention may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic

efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

An antagonist of TRFX may be produced using methods which are generally known in the art. In particular, purified TRFX may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind TRFX. Antibodies to TRFX may also be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments, and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are generally preferred for therapeutic use.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, humans, and others may be immunized by injection with TRFX or with any fragment or oligopeptide thereof which has immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include, but are not limited to, Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially preferable.

It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to TRFX have an amino acid sequence consisting of at least about 5 amino acids, and generally will consist of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein. Short stretches of TRFX amino acids may be fused with those of another protein, such as KLH, and antibodies to the chimeric molecule may be produced.

Monoclonal antibodies to TRFX may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique. (See, e.g., Kohler, G. et al. (1975) Nature 256:495-497; Kozbor, D. et al. (1985) J. Immunol. Methods 81:31-42; Cote, R.J. et al. (1983) Proc. Natl. Acad. Sci. USA 80:2026-2030; and Cole, S.P. et al. (1984) Mol. Cell Biol. 62:109-120.)

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) Proc. Natl. Acad. Sci. USA 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; and Takeda, S. et al. (1985) Nature 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce TRFX-specific single chain antibodies. Antibodies with related specificity, but of distinct idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g.,

Burton, D.R. (1991) Proc. Natl. Acad. Sci. USA 88:10134-10137.)

Antibodies may also be produced by inducing in vivo production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature. (See, e.g., Orlandi, R. et al. (1989) Proc. Natl. Acad. Sci. USA 86:3833-3837; Winter, G. et al. (1991) Nature 349:293-299.)

Antibody fragments which contain specific binding sites for TRFX may also be generated. For example, such fragments include, but are not limited to, $F(ab')_2$ fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the F(ab')2 fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity. (See, e.g., Huse, W.D. et al. (1989) Science 246:1275-1281.)

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between TRFX and its specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering TRFX epitopes is generally used, but a competitive binding assay may also be employed (Pound, supra).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for TRFX. Affinity is expressed as an association constant, K_a, which is defined as the molar concentration of TRFX-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The K_a determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple TRFX epitopes, represents the average affinity, or avidity, of the antibodies for TRFX. The K_a determined for a preparation of monoclonal antibodies, which are monospecific for a particular TRFX epitope, represents a true measure of affinity. High-affinity antibody preparations with K_a ranging from about 10^9 to 10^{12} L/mole are preferred for use in immunoassays in which the TRFX-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with K_a ranging from about 10^6 to 10^7 L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of TRFX, preferably in active form, from the antibody (Catty, D. (1988) Antibodies, Volume I: A Practical Approach, IRL Press, Washington DC; Liddell, J.E. and A. Cryer (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For

example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is generally employed in procedures requiring precipitation of TRFX-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al., supra.)

In another embodiment of the invention, the polynucleotides encoding TRFX, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, modifications of gene expression can be achieved by designing complementary sequences or antisense molecules (DNA, RNA, PNA, or modified oligonucleotides) to the coding or regulatory regions of the gene encoding TRFX. Such technology is well known in the art, and antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding TRFX. (See, e.g., Agrawal, S., ed. (1996) Antisense Therapeutics, Humana Press Inc., Totawa NJ.)

In therapeutic use, any gene delivery system suitable for introduction of the antisense sequences into appropriate target cells can be used. Antisense sequences can be delivered intracellularly in the form of an expression plasmid which, upon transcription, produces a sequence complementary to at least a portion of the cellular sequence encoding the target protein. (See, e.g., Slater, J.E. et al. (1998) J. Allergy Clin. Immunol. 102(3):469-475; and Scanlon, K.J. et al. (1995) 9(13):1288-1296.) Antisense sequences can also be introduced intracellularly through the use of viral vectors, such as retrovirus and adeno-associated virus vectors. (See, e.g., Miller, A.D. (1990) Blood 76:271; Ausubel, supra; Uckert, W. and W. Walther (1994) Pharmacol. Ther. 63(3):323-347.) Other gene delivery mechanisms include liposome-derived systems, artificial viral envelopes, and other systems known in the art. (See, e.g., Rossi, J.J. (1995) Br. Med. Bull. 51(1):217-225; Boado, R.J. et al. (1998) J. Pharm. Sci. 87(11):1308-1315; and Morris, M.C. et al. (1997) Nucleic Acids Res. 25(14):2730-2736.)

In another embodiment of the invention, polynucleotides encoding TRFX may be used for somatic or germline gene therapy. Gene therapy may be performed to (i) correct a genetic deficiency (e.g., in the cases of severe combined immunodeficiency (SCID)-X1 disease characterized by X-linked inheritance (Cavazzana-Calvo, M. et al. (2000) Science 288:669-672), severe combined immunodeficiency syndrome associated with an inherited adenosine deaminase (ADA) deficiency (Blaese, R.M. et al. (1995) Science 270:475-480; Bordignon, C. et al. (1995) Science 270:470-475), cystic fibrosis (Zabner, J. et al. (1993) Cell 75:207-216; Crystal, R.G. et al. (1995) Hum. Gene Therapy 6:643-666; Crystal, R.G. et al. (1995) Hum. Gene Therapy 6:667-703), thalassamias, familial hypercholesterolemia, and hemophilia resulting from Factor VIII or Factor IX deficiencies (Crystal, R.G. (1995) Science 270:404-410; Verma, I.M. and N. Somia (1997) Nature 389:239-242)), (ii)

express a conditionally lethal gene product (e.g., in the case of cancers which result from unregulated cell proliferation), or (iii) express a protein which affords protection against intracellular parasites (e.g., against human retroviruses, such as human immunodeficiency virus (HIV) (Baltimore, D. (1988) Nature 335:395-396; Poeschla, E. et al. (1996) Proc. Natl. Acad. Sci. USA. 93:11395-11399), hepatitis B or C virus (HBV, HCV); fungal parasites, such as Candida albicans and Paracoccidioides brasiliensis; and protozoan parasites such as Plasmodium falciparum and Trypanosoma cruzi). In the case where a genetic deficiency in TRFX expression or regulation causes disease, the expression of TRFX from an appropriate population of transduced cells may alleviate the clinical manifestations caused by the genetic deficiency.

In a further embodiment of the invention, diseases or disorders caused by deficiencies in TRFX are treated by constructing mammalian expression vectors encoding TRFX and introducing these vectors by mechanical means into TRFX-deficient cells. Mechanical transfer technologies for use with cells in vivo or ex vitro include (i) direct DNA microinjection into individual cells, (ii) ballistic gold particle delivery, (iii) liposome-mediated transfection, (iv) receptor-mediated gene transfer, and (v) the use of DNA transposons (Morgan, R.A. and W.F. Anderson (1993) Annu. Rev. Biochem. 62:191-217; Ivics, Z. (1997) Cell 91:501-510; Boulay, J-L. and H. Récipon (1998) Curr. Opin. Biotechnol. 9:445-450).

Expression vectors that may be effective for the expression of TRFX include, but are not limited to, the PCDNA 3.1, EPITAG, PRCCMV2, PREP, PVAX vectors (Invitrogen, Carlsbad CA), PCMV-SCRIPT, PCMV-TAG, PEGSH/PERV (Stratagene, La Jolla CA), and PTET-OFF, PTET-ON, PTRE2, PTRE2-LUC, PTK-HYG (Clontech, Palo Alto CA). TRFX may be expressed using (i) a constitutively active promoter, (e.g., from cytomegalovirus (CMV), Rous sarcoma virus (RSV), SV40 virus, thymidine kinase (TK), or β-actin genes), (ii) an inducible promoter (e.g., the tetracycline-regulated promoter (Gossen, M. and H. Bujard (1992) Proc. Natl. Acad. Sci. USA 89:5547-5551; Gossen, M. et al. (1995) Science 268:1766-1769; Rossi, F.M.V. and H.M. Blau (1998) Curr. Opin. Biotechnol. 9:451-456), commercially available in the T-REX plasmid (Invitrogen)); the ecdysone-inducible promoter (available in the plasmids PVGRXR and PIND; Invitrogen); the FK506/rapamycin inducible promoter; or the RU486/mifepristone inducible promoter (Rossi, F.M.V. and H.M. Blau, supra)), or (iii) a tissue-specific promoter or the native promoter of the endogenous gene encoding TRFX from a normal individual.

Commercially available liposome transformation kits (e.g., the PERFECT LIPID TRANSFECTION KIT, available from Invitrogen) allow one with ordinary skill in the art to deliver polynucleotides to target cells in culture and require minimal effort to optimize experimental parameters. In the alternative, transformation is performed using the calcium phosphate method (Graham, F.L. and A.J. Eb (1973) Virology 52:456-467), or by electroporation (Neumann, E. et al.

(1982) EMBO J. 1:841-845). The introduction of DNA to primary cells requires modification of these standardized mammalian transfection protocols.

In another embodiment of the invention, diseases or disorders caused by genetic defects with respect to TRFX expression are treated by constructing a retrovirus vector consisting of (i) the polynucleotide encoding TRFX under the control of an independent promoter or the retrovirus long terminal repeat (LTR) promoter, (ii) appropriate RNA packaging signals, and (iii) a Rev-responsive element (RRE) along with additional retrovirus *cis*-acting RNA sequences and coding sequences required for efficient vector propagation. Retrovirus vectors (e.g., PFB and PFBNEO) are commercially available (Stratagene) and are based on published data (Riviere, I. et al. (1995) Proc. Natl. Acad. Sci. USA 92:6733-6737), incorporated by reference herein. The vector is propagated in an appropriate vector producing cell line (VPCL) that expresses an envelope gene with a tropism for receptors on the target cells or a promiscuous envelope protein such as VSVg (Armentano, D. et al. (1987) J. Virol. 61:1647-1650; Bender, M.A. et al. (1987) J. Virol. 61:1639-1646; Adam, M.A. and A.D. Miller (1988) J. Virol. 62:3802-3806; Dull, T. et al. (1998) J. Virol. 72:8463-8471; Zufferey, R. et al. (1998) J. Virol. 72:9873-9880). U.S. Patent Number 5,910,434 to Rigg ("Method for obtaining retrovirus packaging cell lines producing high transducing efficiency retroviral supernatant") discloses a method for obtaining retrovirus packaging cell lines and is hereby incorporated by reference. Propagation of retrovirus vectors, transduction of a population of cells (e.g., $CD4^+$ T-cells), and the return of transduced cells to a patient are procedures well known to persons skilled in the art of gene therapy and have been well documented (Ranga, U. et al. (1997) J. Virol. 71:7020-7029; Bauer, G. et al. (1997) Blood 89:2259-2267; Bonyhadi, M.L. (1997) J. Virol. 71:4707-4716; Ranga, U. et al. (1998) Proc. Natl. Acad. Sci. USA 95:1201-1206; Su, L. (1997) Blood 89:2283-2290).

In the alternative, an adenovirus-based gene therapy delivery system is used to deliver polynucleotides encoding TRFX to cells which have one or more genetic abnormalities with respect to the expression of TRFX. The construction and packaging of adenovirus-based vectors are well known to those with ordinary skill in the art. Replication defective adenovirus vectors have proven to be versatile for importing genes encoding immunoregulatory proteins into intact islets in the pancreas (Csete, M.E. et al. (1995) Transplantation 27:263-268). Potentially useful adenoviral vectors are described in U.S. Patent Number 5,707,618 to Armentano ("Adenovirus vectors for gene therapy"), hereby incorporated by reference. For adenoviral vectors, see also Antinozzi, P.A. et al. (1999) Annu. Rev. Nutr. 19:511-544; and Verma, I.M. and N. Somia (1997) Nature 18:389:239-242, both incorporated by reference herein.

In another alternative, a herpes-based, gene therapy delivery system is used to deliver polynucleotides encoding TRFX to target cells which have one or more genetic abnormalities with

respect to the expression of TRFX. The use of herpes simplex virus (HSV)-based vectors may be especially valuable for introducing TRFX to cells of the central nervous system, for which HSV has a tropism. The construction and packaging of herpes-based vectors are well known to those with ordinary skill in the art. A replication-competent herpes simplex virus (HSV) type 1-based vector has been used to deliver a reporter gene to the eyes of primates (Liu, X. et al. (1999) Exp. Eye Res. 169:385-395). The construction of a HSV-1 virus vector has also been disclosed in detail in U.S. Patent Number 5,804,413 to DeLuca ("Herpes simplex virus strains for gene transfer"), which is hereby incorporated by reference. U.S. Patent Number 5,804,413 teaches the use of recombinant HSV d92 which consists of a genome containing at least one exogenous gene to be transferred to a cell under the control of the appropriate promoter for purposes including human gene therapy. Also taught by this patent are the construction and use of recombinant HSV strains deleted for ICP4, ICP27 and ICP22. For HSV vectors, see also Goins, W.F. et al. (1999) J. Virol. 73:519-532 and Xu, H. et al. (1994) Dev. Biol. 163:152-161, hereby incorporated by reference. The manipulation of cloned herpesvirus sequences, the generation of recombinant virus following the transfection of multiple plasmids containing different segments of the large herpesvirus genomes, the growth and propagation of herpesvirus, and the infection of cells with herpesvirus are techniques well known to those of ordinary skill in the art.

In another alternative, an alphavirus (positive, single-stranded RNA virus) vector is used to deliver polynucleotides encoding TRFX to target cells. The biology of the prototypic alphavirus, Semliki Forest Virus (SFV), has been studied extensively and gene transfer vectors have been based on the SFV genome (Garoff, H. and K.-J. Li (1998) Curr. Opin. Biotechnol. 9:464-469). During alphavirus RNA replication, a subgenomic RNA is generated that normally encodes the viral capsid proteins. This subgenomic RNA replicates to higher levels than the full-length genomic RNA, resulting in the overproduction of capsid proteins relative to the viral proteins with enzymatic activity (e.g., protease and polymerase). Similarly, inserting the coding sequence for TRFX into the alphavirus genome in place of the capsid-coding region results in the production of a large number of TRFX-coding RNAs and the synthesis of high levels of TRFX in vector transduced cells. While alphavirus infection is typically associated with cell lysis within a few days, the ability to establish a persistent infection in hamster normal kidney cells (BHK-21) with a variant of Sindbis virus (SIN) indicates that the lytic replication of alphaviruses can be altered to suit the needs of the gene therapy application (Dryga, S.A. et al. (1997) Virology 228:74-83). The wide host range of alphaviruses will allow the introduction of TRFX into a variety of cell types. The specific transduction of a subset of cells in a population may require the sorting of cells prior to transduction. The methods of manipulating infectious cDNA clones of alphaviruses, performing alphavirus cDNA and RNA transfections, and performing alphavirus infections, are well known to those with ordinary skill in the

art.

Oligonucleotides derived from the transcription initiation site, e.g., between about positions -10 and +10 from the start site, may also be employed to inhibit gene expression. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature. (See, e.g., Gee, J.E. et al. (1994) in Huber, B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177.) A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze endonucleolytic cleavage of sequences encoding TRFX.

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides, corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

Complementary ribonucleic acid molecules and ribozymes of the invention may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by in vitro and in vivo transcription of DNA sequences encoding TRFX. Such DNA sequences may be incorporated into a wide variety of vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine,

queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

An additional embodiment of the invention encompasses a method for screening for a compound which is effective in altering expression of a polynucleotide encoding TRFX. Compounds which may be effective in altering expression of a specific polynucleotide may include, but are not limited to, oligonucleotides, antisense oligonucleotides, triple helix-forming oligonucleotides, transcription factors and other polypeptide transcriptional regulators, and non-macromolecular chemical entities which are capable of interacting with specific polynucleotide sequences. Effective compounds may alter polynucleotide expression by acting as either inhibitors or promoters of polynucleotide expression. Thus, in the treatment of disorders associated with increased TRFX expression or activity, a compound which specifically inhibits expression of the polynucleotide encoding TRFX may be therapeutically useful, and in the treament of disorders associated with decreased TRFX expression or activity, a compound which specifically promotes expression of the polynucleotide encoding TRFX may be therapeutically useful.

At least one, and up to a plurality, of test compounds may be screened for effectiveness in altering expression of a specific polynucleotide. A test compound may be obtained by any method commonly known in the art, including chemical modification of a compound known to be effective in altering polynucleotide expression; selection from an existing, commercially-available or proprietary library of naturally-occurring or non-natural chemical compounds; rational design of a compound based on chemical and/or structural properties of the target polynucleotide; and selection from a library of chemical compounds created combinatorially or randomly. A sample comprising a polynucleotide encoding TRFX is exposed to at least one test compound thus obtained. The sample may comprise, for example, an intact or permeabilized cell, or an in vitro cell-free or reconstituted biochemical system. Alterations in the expression of a polynucleotide encoding TRFX are assayed by any method commonly known in the art. Typically, the expression of a specific nucleotide is detected by hybridization with a probe having a nucleotide sequence complementary to the sequence of the polynucleotide encoding TRFX. The amount of hybridization may be quantified, thus forming the basis for a comparison of the expression of the polynucleotide both with and without exposure to one or more test compounds. Detection of a change in the expression of a polynucleotide exposed to a test compound indicates that the test compound is effective in altering the expression of the polynucleotide. A screen for a compound effective in altering expression of a specific polynucleotide can be carried out, for example, using a Schizosaccharomyces pombe gene expression system (Atkins, D. et al. (1999) U.S. Patent No. 5,932,435; Arndt, G.M. et al. (2000) Nucleic Acids Res.

28:E15) or a human cell line such as HeLa cell (Clarke, M.L. et al. (2000) Biochem. Biophys. Res. Commun. 268:8-13). A particular embodiment of the present invention involves screening a combinatorial library of oligonucleotides (such as deoxyribonucleotides, ribonucleotides, peptide nucleic acids, and modified oligonucleotides) for antisense activity against a specific polynucleotide sequence (Bruice, T.W. et al. (1997) U.S. Patent No. 5,686,242; Bruice, T.W. et al. (2000) U.S. Patent No. 6,022,691).

Many methods for introducing vectors into cells or tissues are available and equally suitable for use in vivo, in vitro, and ex vivo. For ex vivo therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or by polycationic amino polymers may be achieved using methods which are well known in the art. (See, e.g., Goldman, C.K. et al. (1997) Nat. Biotechnol. 15:462-466.)

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as humans, dogs, cats, cows, horses, rabbits, and monkeys.

An additional embodiment of the invention relates to the administration of a composition which generally comprises an active ingredient formulated with a pharmaceutically acceptable excipient. Excipients may include, for example, sugars, starches, celluloses, gums, and proteins. Various formulations are commonly known and are thoroughly discussed in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing, Easton PA). Such compositions may consist of TRFX, antibodies to TRFX, and mimetics, agonists, antagonists, or inhibitors of TRFX.

The compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, pulmonary, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

Compositions for pulmonary administration may be prepared in liquid or dry powder form. These compositions are generally aerosolized immediately prior to inhalation by the patient. In the case of small molecules (e.g. traditional low molecular weight organic drugs), aerosol delivery of fast-acting formulations is well-known in the art. In the case of macromolecules (e.g. larger peptides and proteins), recent developments in the field of pulmonary delivery via the alveolar region of the lung have enabled the practical delivery of drugs such as insulin to blood circulation (see, e.g., Patton, J.S. et al., U.S. Patent No. 5,997,848). Pulmonary delivery has the advantage of administration without needle injection, and obviates the need for potentially toxic penetration enhancers.

Compositions suitable for use in the invention include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The determination

of an effective dose is well within the capability of those skilled in the art.

Specialized forms of compositions may be prepared for direct intracellular delivery of macromolecules comprising TRFX or fragments thereof. For example, liposome preparations containing a cell-impermeable macromolecule may promote cell fusion and intracellular delivery of the macromolecule. Alternatively, TRFX or a fragment thereof may be joined to a short cationic N-terminal portion from the HIV Tat-1 protein. Fusion proteins thus generated have been found to transduce into the cells of all tissues, including the brain, in a mouse model system (Schwarze, S.R. et al. (1999) Science 285:1569-1572).

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells, or in animal models such as mice, rats, rabbits, dogs, monkeys, or pigs. An animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example TRFX or fragments thereof, antibodies of TRFX, and agonists, antagonists or inhibitors of TRFX, which ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the ED_{50} (the dose therapeutically effective in 50% of the population) or LD_{50} (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as the LD_{50}/ED_{50} ratio. Compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the ED_{50} with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy. Long-acting compositions may be administered every 3 to 4 days, every week, or biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about 0.1 μg to 100,000 μg, up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art.

Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

DIAGNOSTICS

In another embodiment, antibodies which specifically bind TRFX may be used for the diagnosis of disorders characterized by expression of TRFX, or in assays to monitor patients being treated with TRFX or agonists, antagonists, or inhibitors of TRFX. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics. Diagnostic assays for TRFX include methods which utilize the antibody and a label to detect TRFX in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled by covalent or non-covalent attachment of a reporter molecule. A wide variety of reporter molecules, several of which are described above, are known in the art and may be used.

A variety of protocols for measuring TRFX, including ELISAs, RIAs, and FACS, are known in the art and provide a basis for diagnosing altered or abnormal levels of TRFX expression. Normal or standard values for TRFX expression are established by combining body fluids or cell extracts taken from normal mammalian subjects, for example, human subjects, with antibody to TRFX under conditions suitable for complex formation. The amount of standard complex formation may be quantitated by various methods, such as photometric means. Quantities of TRFX expressed in subject, control, and disease samples from biopsied tissues are compared with the standard values. Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, the polynucleotides encoding TRFX may be used for diagnostic purposes. The polynucleotides which may be used include oligonucleotide sequences, complementary RNA and DNA molecules, and PNAs. The polynucleotides may be used to detect and quantify gene expression in biopsied tissues in which expression of TRFX may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of TRFX, and to monitor regulation of TRFX levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting polynucleotide sequences, including genomic sequences, encoding TRFX or closely related molecules may be used to identify nucleic acid sequences which encode TRFX. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a conserved motif, and the stringency of the hybridization or amplification will determine whether the probe identifies only naturally occurring sequences encoding TRFX, allelic variants, or related sequences.

Probes may also be used for the detection of related sequences, and may have at least 50% sequence identity to any of the TRFX encoding sequences. The hybridization probes of the subject

invention may be DNA or RNA and may be derived from the sequence of SEQ ID NO:108-214 or from genomic sequences including promoters, enhancers, and introns of the TRFX gene.

Means for producing specific hybridization probes for DNAs encoding TRFX include the cloning of polynucleotide sequences encoding TRFX or TRFX derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, by radionuclides such as ^{32}P or ^{35}S, or by enzymatic labels, such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotide sequences encoding TRFX may be used for the diagnosis of disorders associated with expression of TRFX. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; an autoimmune/inflammatory disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; a neurological disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and

other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system including Down syndrome, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, seasonal affective disorder (SAD), akathesia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, Tourette's disorder, progressive supranuclear palsy, corticobasal degeneration, and familial frontotemporal dementia; and a developmental disorder such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy, gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and mental retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratodermas, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Syndenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract, and sensorineural hearing loss. The polynucleotide sequences encoding TRFX may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered TRFX expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, the nucleotide sequences encoding TRFX may be useful in assays that detect the presence of associated disorders, particularly those mentioned above. The nucleotide sequences encoding TRFX may be labeled by standard methods and added to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantified and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence of altered levels of nucleotide sequences encoding TRFX in the sample indicates the presence of the associated disorder. Such assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with expression of TRFX, a normal or standard profile for expression is established. This may be accomplished by combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding TRFX, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an experiment in which a known amount of a substantially purified polynucleotide is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated, hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Additional diagnostic uses for oligonucleotides designed from the sequences encoding TRFX may involve the use of PCR. These oligomers may be chemically synthesized, generated enzymatically, or produced in vitro. Oligomers will preferably contain a fragment of a polynucleotide encoding TRFX, or a fragment of a polynucleotide complementary to the polynucleotide encoding TRFX, and will be employed under optimized conditions for identification of a specific gene or condition. Oligomers may also be employed under less stringent conditions for detection or quantification of closely related DNA or RNA sequences.

In a particular aspect, oligonucleotide primers derived from the polynucleotide sequences encoding TRFX may be used to detect single nucleotide polymorphisms (SNPs). SNPs are substitutions, insertions and deletions that are a frequent cause of inherited or acquired genetic disease in humans. Methods of SNP detection include, but are not limited to, single-stranded conformation polymorphism (SSCP) and fluorescent SSCP (fSSCP) methods. In SSCP, oligonucleotide primers derived from the polynucleotide sequences encoding TRFX are used to amplify DNA using the polymerase chain reaction (PCR). The DNA may be derived, for example, from diseased or normal tissue, biopsy samples, bodily fluids, and the like. SNPs in the DNA cause

differences in the secondary and tertiary structures of PCR products in single-stranded form, and these differences are detectable using gel electrophoresis in non-denaturing gels. In fSCCP, the oligonucleotide primers are fluorescently labeled, which allows detection of the amplimers in high-throughput equipment such as DNA sequencing machines. Additionally, sequence database analysis methods, termed in silico SNP (isSNP), are capable of identifying polymorphisms by comparing the sequence of individual overlapping DNA fragments which assemble into a common consensus sequence. These computer-based methods filter out sequence variations due to laboratory preparation of DNA and sequencing errors using statistical models and automated analyses of DNA sequence chromatograms. In the alternative, SNPs may be detected and characterized by mass spectrometry using, for example, the high throughput MASSARRAY system (Sequenom, Inc., San Diego CA).

Methods which may also be used to quantify the expression of TRFX include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves. (See, e.g., Melby, P.C. et al. (1993) J. Immunol. Methods 159:235-244; Duplaa, C. et al. (1993) Anal. Biochem. 212:229-236.) The speed of quantitation of multiple samples may be accelerated by running the assay in a high-throughput format where the oligomer or polynucleotide of interest is presented in various dilutions and a spectrophotometric or colorimetric response gives rapid quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of the polynucleotide sequences described herein may be used as elements on a microarray. The microarray can be used in transcript imaging techniques which monitor the relative expression levels of large numbers of genes simultaneously as described in Seilhamer, J.J. et al., "Comparative Gene Transcript Analysis," U.S. Patent No. 5,840,484, incorporated herein by reference. The microarray may also be used to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, to monitor progression/regression of disease as a function of gene expression, and to develop and monitor the activities of therapeutic agents in the treatment of disease. In particular, this information may be used to develop a pharmacogenomic profile of a patient in order to select the most appropriate and effective treatment regimen for that patient. For example, therapeutic agents which are highly effective and display the fewest side effects may be selected for a patient based on his/her pharmacogenomic profile.

In another embodiment, antibodies specific for TRFX, or TRFX or fragments thereof may be used as elements on a microarray. The microarray may be used to monitor or measure protein-protein interactions, drug-target interactions, and gene expression profiles, as described above.

A particular embodiment relates to the use of the polynucleotides of the present invention to generate a transcript image of a tissue or cell type. A transcript image represents the global pattern of

gene expression by a particular tissue or cell type. Global gene expression patterns are analyzed by quantifying the number of expressed genes and their relative abundance under given conditions and at a given time. (See Seilhamer et al., "Comparative Gene Transcript Analysis," U.S. Patent Number 5,840,484, expressly incorporated by reference herein.) Thus a transcript image may be generated by hybridizing the polynucleotides of the present invention or their complements to the totality of transcripts or reverse transcripts of a particular tissue or cell type. In one embodiment, the hybridization takes place in high-throughput format, wherein the polynucleotides of the present invention or their complements comprise a subset of a plurality of elements on a microarray. The resultant transcript image would provide a profile of gene activity.

Transcript images may be generated using transcripts isolated from tissues, cell lines, biopsies, or other biological samples. The transcript image may thus reflect gene expression in vivo, as in the case of a tissue or biopsy sample, or in vitro, as in the case of a cell line.

Transcript images which profile the expression of the polynucleotides of the present invention may also be used in conjunction with in vitro model systems and preclinical evaluation of pharmaceuticals, as well as toxicological testing of industrial and naturally-occurring environmental compounds. All compounds induce characteristic gene expression patterns, frequently termed molecular fingerprints or toxicant signatures, which are indicative of mechanisms of action and toxicity (Nuwaysir, E.F. et al. (1999) Mol. Carcinog. 24:153-159; Steiner, S. and N.L. Anderson (2000) Toxicol. Lett. 112-113:467-471, expressly incorporated by reference herein). If a test compound has a signature similar to that of a compound with known toxicity, it is likely to share those toxic properties. These fingerprints or signatures are most useful and refined when they contain expression information from a large number of genes and gene families. Ideally, a genome-wide measurement of expression provides the highest quality signature. Even genes whose expression is not altered by any tested compounds are important as well, as the levels of expression of these genes are used to normalize the rest of the expression data. The normalization procedure is useful for comparison of expression data after treatment with different compounds. While the assignment of gene function to elements of a toxicant signature aids in interpretation of toxicity mechanisms, knowledge of gene function is not necessary for the statistical matching of signatures which leads to prediction of toxicity. (See, for example, Press Release 00-02 from the National Institute of Environmental Health Sciences, released February 29, 2000, available at http://www.niehs.nih.gov/oc/news/toxchip.htm.) Therefore, it is important and desirable in toxicological screening using toxicant signatures to include all expressed gene sequences.

In one embodiment, the toxicity of a test compound is assessed by treating a biological sample containing nucleic acids with the test compound. Nucleic acids that are expressed in the treated biological sample are hybridized with one or more probes specific to the polynucleotides of

the present invention, so that transcript levels corresponding to the polynucleotides of the present invention may be quantified. The transcript levels in the treated biological sample are compared with levels in an untreated biological sample. Differences in the transcript levels between the two samples are indicative of a toxic response caused by the test compound in the treated sample.

Another particular embodiment relates to the use of the polypeptide sequences of the present invention to analyze the proteome of a tissue or cell type. The term proteome refers to the global pattern of protein expression in a particular tissue or cell type. Each protein component of a proteome can be subjected individually to further analysis. Proteome expression patterns, or profiles, are analyzed by quantifying the number of expressed proteins and their relative abundance under given conditions and at a given time. A profile of a cell's proteome may thus be generated by separating and analyzing the polypeptides of a particular tissue or cell type. In one embodiment, the separation is achieved using two-dimensional gel electrophoresis, in which proteins from a sample are separated by isoelectric focusing in the first dimension, and then according to molecular weight by sodium dodecyl sulfate slab gel electrophoresis in the second dimension (Steiner and Anderson, supra). The proteins are visualized in the gel as discrete and uniquely positioned spots, typically by staining the gel with an agent such as Coomassie Blue or silver or fluorescent stains. The optical density of each protein spot is generally proportional to the level of the protein in the sample. The optical densities of equivalently positioned protein spots from different samples, for example, from biological samples either treated or untreated with a test compound or therapeutic agent, are compared to identify any changes in protein spot density related to the treatment. The proteins in the spots are partially sequenced using, for example, standard methods employing chemical or enzymatic cleavage followed by mass spectrometry. The identity of the protein in a spot may be determined by comparing its partial sequence, preferably of at least 5 contiguous amino acid residues, to the polypeptide sequences of the present invention. In some cases, further sequence data may be obtained for definitive protein identification.

A proteomic profile may also be generated using antibodies specific for TRFX to quantify the levels of TRFX expression. In one embodiment, the antibodies are used as elements on a microarray, and protein expression levels are quantified by exposing the microarray to the sample and detecting the levels of protein bound to each array element (Lueking, A. et al. (1999) Anal. Biochem. 270:103-111; Mendoze, L.G. et al. (1999) Biotechniques 27:778-788). Detection may be performed by a variety of methods known in the art, for example, by reacting the proteins in the sample with a thiol- or amino-reactive fluorescent compound and detecting the amount of fluorescence bound at each array element.

Toxicant signatures at the proteome level are also useful for toxicological screening, and should be analyzed in parallel with toxicant signatures at the transcript level. There is a poor

correlation between transcript and protein abundances for some proteins in some tissues (Anderson, N.L. and J. Seilhamer (1997) Electrophoresis 18:533-537), so proteome toxicant signatures may be useful in the analysis of compounds which do not significantly affect the transcript image, but which alter the proteomic profile. In addition, the analysis of transcripts in body fluids is difficult, due to rapid degradation of mRNA, so proteomic profiling may be more reliable and informative in such cases.

In another embodiment, the toxicity of a test compound is assessed by treating a biological sample containing proteins with the test compound. Proteins that are expressed in the treated biological sample are separated so that the amount of each protein can be quantified. The amount of each protein is compared to the amount of the corresponding protein in an untreated biological sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound in the treated sample. Individual proteins are identified by sequencing the amino acid residues of the individual proteins and comparing these partial sequences to the polypeptides of the present invention.

In another embodiment, the toxicity of a test compound is assessed by treating a biological sample containing proteins with the test compound. Proteins from the biological sample are incubated with antibodies specific to the polypeptides of the present invention. The amount of protein recognized by the antibodies is quantified. The amount of protein in the treated biological sample is compared with the amount in an untreated biological sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound in the treated sample.

Microarrays may be prepared, used, and analyzed using methods known in the art. (See, e.g., Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl. Acad. Sci. USA 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al. (1997) Proc. Natl. Acad. Sci. USA 94:2150-2155; and Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662.) Various types of microarrays are well known and thoroughly described in DNA Microarrays: A Practical Approach, M. Schena, ed. (1999) Oxford University Press, London, hereby expressly incorporated by reference.

In another embodiment of the invention, nucleic acid sequences encoding TRFX may be used to generate hybridization probes useful in mapping the naturally occurring genomic sequence. Either coding or noncoding sequences may be used, and in some instances, noncoding sequences may be preferable over coding sequences. For example, conservation of a coding sequence among members of a multi-gene family may potentially cause undesired cross hybridization during chromosomal mapping. The sequences may be mapped to a particular chromosome, to a specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs),

yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single chromosome cDNA libraries. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355; Price, C.M. (1993) Blood Rev. 7:127-134; and Trask, B.J. (1991) Trends Genet. 7:149-154.) Once mapped, the nucleic acid sequences of the invention may be used to develop genetic linkage maps, for example, which correlate the inheritance of a disease state with the inheritance of a particular chromosome region or restriction fragment length polymorphism (RFLP). (See, e.g., Lander, E.S. and D. Botstein (1986) Proc. Natl. Acad. Sci. USA 83:7353-7357.)

Fluorescent in situ hybridization (FISH) may be correlated with other physical and genetic map data. (See, e.g., Heinz-Ulrich, et al. (1995) in Meyers, supra, pp. 965-968.) Examples of genetic map data can be found in various scientific journals or at the Online Mendelian Inheritance in Man (OMIM) World Wide Web site. Correlation between the location of the gene encoding TRFX on a physical map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder and thus may further positional cloning efforts.

In situ hybridization of chromosomal preparations and physical mapping techniques, such as linkage analysis using established chromosomal markers, may be used for extending genetic maps. Often the placement of a gene on the chromosome of another mammalian species, such as mouse, may reveal associated markers even if the exact chromosomal locus is not known. This information is valuable to investigators searching for disease genes using positional cloning or other gene discovery techniques. Once the gene or genes responsible for a disease or syndrome have been crudely localized by genetic linkage to a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23, any sequences mapping to that area may represent associated or regulatory genes for further investigation. (See, e.g., Gatti, R.A. et al. (1988) Nature 336:577-580.) The nucleotide sequence of the instant invention may also be used to detect differences in the chromosomal location due to translocation, inversion, etc., among normal, carrier, or affected individuals.

In another embodiment of the invention, TRFX, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes between TRFX and the agent being tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest. (See, e.g., Geysen, et al. (1984) PCT application WO84/03564.) In this method, large numbers of different small test compounds are synthesized on a solid substrate. The test compounds are reacted with TRFX, or fragments thereof, and washed. Bound TRFX is then detected by methods well known in the art. Purified TRFX can also be coated directly onto plates for use in the aforementioned drug screening techniques.

Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

In another embodiment, one may use competitive drug screening assays in which neutralizing antibodies capable of binding TRFX specifically compete with a test compound for binding TRFX. In this manner, antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with TRFX.

In additional embodiments, the nucleotide sequences which encode TRFX may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely on properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair interactions.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

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The disclosures of all patents, applications, and publications mentioned above and below, in particular U.S. Ser. No. 60/188,986, are hereby expressly incorporated by reference.

EXAMPLES

I. Construction of cDNA Libraries

RNA was purchased from Clontech or isolated from tissues described in Table 4. Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed in phenol or in a suitable mixture of denaturants, such as TRIZOL (Life Technologies), a monophasic solution of phenol and guanidine isothiocyanate. The resulting lysates were centrifuged over CsCl cushions or extracted with chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA purity. In some cases, RNA was treated with DNase. For most libraries, poly(A+) RNA was isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN, Chatsworth CA), or an OLIGOTEX mRNA purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

In some cases, Stratagene was provided with RNA and constructed the corresponding cDNA libraries. Otherwise, cDNA was synthesized and cDNA libraries were constructed with the UNIZAP vector system (Stratagene) or SUPERSCRIPT plasmid system (Life Technologies), using the recommended procedures or similar methods known in the art. (See, e.g., Ausubel, 1997, supra, units 5.1-6.6.) Reverse transcription was initiated using oligo d(T) or random primers. Synthetic oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA was digested with the appropriate restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000, SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Pharmacia Biotech) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g., PBLUESCRIPT plasmid (Stratagene), PSPORT1 plasmid (Life Technologies), pcDNA2.1 plasmid (Invitrogen, Carlsbad CA), or pINCY plasmid (Incyte Genomics, Palo Alto CA). Recombinant plasmids were transformed into competent E. coli cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5α, DH10B, or ElectroMAX DH10B from Life Technologies.

II. Isolation of cDNA Clones

Plasmids obtained as described in Example I were recovered from host cells by in vivo excision using the UNIZAP vector system (Stratagene) or by cell lysis. Plasmids were purified using at least one of the following: a Magic or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plus Plasmid, QIAWELL 8 Ultra Plasmid purification systems or the R.E.A.L. PREP 96 plasmid purification kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1 ml of distilled water and stored, with or without lyophilization, at 4°C.

Alternatively, plasmid DNA was amplified from host cell lysates using direct link PCR in a high-throughput format (Rao, V.B. (1994) Anal. Biochem. 216:1-14). Host cell lysis and thermal cycling steps were carried out in a single reaction mixture. Samples were processed and stored in 384-well plates, and the concentration of amplified plasmid DNA was quantified fluorometrically using PICOGREEN dye (Molecular Probes, Eugene OR) and a FLUOROSKAN II fluorescence scanner (Labsystems Oy, Helsinki, Finland).

III. Sequencing and Analysis

Incyte cDNA recovered in plasmids as described in Example II were sequenced as follows. Sequencing reactions were processed using standard methods or high-throughput instrumentation such as the ABI CATALYST 800 (Applied Biosystems) thermal cycler or the PTC-200 thermal cycler (MJ Research) in conjunction with the HYDRA microdispenser (Robbins Scientific) or the MICROLAB 2200 (Hamilton) liquid transfer system. cDNA sequencing reactions were prepared using reagents provided by Amersham Pharmacia Biotech or supplied in ABI sequencing kits such as

the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Applied Biosystems). Electrophoretic separation of cDNA sequencing reactions and detection of labeled polynucleotides were carried out using the MEGABACE 1000 DNA sequencing system (Molecular Dynamics); the ABI PRISM 373 or 377 sequencing system (Applied Biosystems) in conjunction with standard ABI protocols and base calling software; or other sequence analysis systems known in the art. Reading frames within the cDNA sequences were identified using standard methods (reviewed in Ausubel, 1997, supra, unit 7.7). Some of the cDNA sequences were selected for extension using the techniques disclosed in Example VI.

The polynucleotide sequences derived from cDNA sequencing were assembled and analyzed using a combination of software programs which utilize algorithms well known to those skilled in the art. Table 5 summarizes the tools, programs, and algorithms used and provides applicable descriptions, references, and threshold parameters. The first column of Table 5 shows the tools, programs, and algorithms used, the second column provides brief descriptions thereof, the third column presents appropriate references, all of which are incorporated by reference herein in their entirety, and the fourth column presents, where applicable, the scores, probability values, and other parameters used to evaluate the strength of a match between two sequences (the higher the score, the greater the homology between two sequences). Sequences were analyzed using MACDNASIS PRO software (Hitachi Software Engineering, South San Francisco CA) and LASERGENE software (DNASTAR). Polynucleotide and polypeptide sequence alignments were generated using the default parameters specified by the clustal algorithm as incorporated into the MEGALIGN multisequence alignment program (DNASTAR), which also calculates the percent identity between aligned sequences.

The polynucleotide sequences were validated by removing vector, linker, and polyA sequences and by masking ambiguous bases, using algorithms and programs based on BLAST, dynamic programing, and dinucleotide nearest neighbor analysis. The sequences were then queried against a selection of public databases such as the GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS, PRINTS, DOMO, PRODOM, and PFAM to acquire annotation using programs based on BLAST, FASTA, and BLIMPS. The sequences were assembled into full length polynucleotide sequences using programs based on Phred, Phrap, and Consed, and were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length amino acid sequences, and these full length sequences were subsequently analyzed by querying against databases such as the GenBank databases (described above), SwissProt, BLOCKS, PRINTS, DOMO, PRODOM, Prosite, and Hidden Markov Model (HMM)-based protein family databases such as PFAM. HMM is a probabilistic approach which analyzes consensus primary structures of gene

families. (See, e.g., Eddy, S.R. (1996) Curr. Opin. Struct. Biol. 6:361-365.)

The programs described above for the assembly and analysis of full length polynucleotide and amino acid sequences were also used to identify polynucleotide sequence fragments from SEQ ID NO:108-214. Fragments from about 20 to about 4000 nucleotides which are useful in hybridization and amplification technologies were described in The Invention section above.

IV. Analysis of Polynucleotide Expression

Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound. (See, e.g., Sambrook, supra, ch. 7; Ausubel, 1995, supra, ch. 4 and 16.)

Analogous computer techniques applying BLAST were used to search for identical or related molecules in cDNA databases such as GenBank or LIFESEQ (Incyte Genomics). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any particular match is categorized as exact or similar. The basis of the search is the product score, which is defined as:

$$\frac{\text{BLAST Score x Percent Identity}}{5 \text{ x minimum }\{\text{length(Seq. 1), length(Seq. 2)}\}}$$

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. The product score is a normalized value between 0 and 100, and is calculated as follows: the BLAST score is multiplied by the percent nucleotide identity and the product is divided by (5 times the length of the shorter of the two sequences). The BLAST score is calculated by assigning a score of +5 for every base that matches in a high-scoring segment pair (HSP), and -4 for every mismatch. Two sequences may share more than one HSP (separated by gaps). If there is more than one HSP, then the pair with the highest BLAST score is used to calculate the product score. The product score represents a balance between fractional overlap and quality in a BLAST alignment. For example, a product score of 100 is produced only for 100% identity over the entire length of the shorter of the two sequences being compared. A product score of 70 is produced either by 100% identity and 70% overlap at one end, or by 88% identity and 100% overlap at the other. A product score of 50 is produced either by 100% identity and 50% overlap at one end, or 79% identity and 100% overlap.

The results of northern analyses are reported as a percentage distribution of libraries in which the transcript encoding TRFX occurred. Analysis involved the categorization of cDNA libraries by organ/tissue and disease. The organ/tissue categories included cardiovascular, dermatologic, developmental, endocrine, gastrointestinal, hematopoietic/immune, musculoskeletal, nervous,

reproductive, and urologic. The disease/condition categories included cancer, inflammation, trauma, cell proliferation, neurological, and pooled. For each category, the number of libraries expressing the sequence of interest was counted and divided by the total number of libraries across all categories. Percentage values of tissue-specific and disease- or condition-specific expression are reported in Table 3.

V. Chromosomal Mapping of TRFX Encoding Polynucleotides

The cDNA sequences which were used to assemble SEQ ID NO:108-214 were compared with sequences from the Incyte LIFESEQ database and public domain databases using BLAST and other implementations of the Smith-Waterman algorithm. Sequences from these databases that matched SEQ ID NO:108-214 were assembled into clusters of contiguous and overlapping sequences using assembly algorithms such as Phrap (Table 5). Radiation hybrid and genetic mapping data available from public resources such as the Stanford Human Genome Center (SHGC), Whitehead Institute for Genome Research (WIGR), and Généthon were used to determine if any of the clustered sequences had been previously mapped. Inclusion of a mapped sequence in a cluster resulted in the assignment of all sequences of that cluster, including its particular SEQ ID NO:, to that map location.

The genetic map locations of SEQ ID NO:111, 114, 117, 122, 123, 125, 130, 132-134, 136, 138, 145, 149, 152, 153, 156, 159, 168, 179, 180, 184, 185, 196, 197, 199, 201, 204, 208, 212, and 213, are described in The Invention as ranges, or intervals, of human chromosomes. More than one map location is reported for SEQ ID NO:145, 152, 184, 185, 199, 208, and 212, indicating that previously mapped sequences having similarity, but not complete identity, to SEQ ID NO:145, 152, 184, 185, 199, 208, and 212 were assembled into their respective clusters. The map position of an interval, in centiMorgans, is measured relative to the terminus of the chromosome's p-arm. (The centiMorgan (cM) is a unit of measurement based on recombination frequencies between chromosomal markers. On average, 1 cM is roughly equivalent to 1 megabase (Mb) of DNA in humans, although this can vary widely due to hot and cold spots of recombination.) The cM distances are based on genetic markers mapped by Généthon which provide boundaries for radiation hybrid markers whose sequences were included in each of the clusters. Human genome maps and other resources available to the public, such as the NCBI "GeneMap'99" World Wide Web site (http://www.ncbi.nlm.nih.gov/genemap/), can be employed to determine if previously identified disease genes map within or in proximity to the intervals indicated above.

VI. Extension of TRFX Encoding Polynucleotides

The full length nucleic acid sequences of SEQ ID NO:108-214 were produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the

other primer, to initiate 3' extension of the known fragment. The initial primers were designed using OLIGO 4.06 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

Selected human cDNA libraries were used to extend the sequence. If more than one extension was necessary or desired, additional or nested sets of primers were designed.

High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer, reaction buffer containing Mg^{2+}, $(NH_4)_2SO_4$, and β-mercaptoethanol, Taq DNA polymerase (Amersham Pharmacia Biotech), ELONGASE enzyme (Life Technologies), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C. In the alternative, the parameters for primer pair T7 and SK+ were as follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C.

The concentration of DNA in each well was determined by dispensing 100 μl PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene OR) dissolved in 1X TE and 0.5 μl of undiluted PCR product into each well of an opaque fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent. The plate was scanned in a Fluoroskan II (Labsystems Oy, Helsinki, Finland) to measure the fluorescence of the sample and to quantify the concentration of DNA. A 5 μl to 10 μl aliquot of the reaction mixture was analyzed by electrophoresis on a 1 % agarose mini-gel to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well plates, digested with CviJI cholera virus endonuclease (Molecular Biology Research, Madison WI), and sonicated or sheared prior to religation into pUC 18 vector (Amersham Pharmacia Biotech). For shotgun sequencing, the digested nucleotides were separated on low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England Biolabs, Beverly MA) into pUC 18 vector (Amersham Pharmacia Biotech), treated with Pfu DNA polymerase (Stratagene) to fill-in restriction site overhangs, and transfected into competent E. coli cells. Transformed cells were selected on antibiotic-containing media, and individual colonies were picked and cultured overnight at 37°C in 384-well plates in LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA polymerase (Amersham Pharmacia Biotech) and Pfu DNA polymerase (Stratagene) with the following parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 72°C, 2 min; Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step 7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as described above. Samples with low DNA recoveries were reamplified using the same conditions as described above. Samples were diluted with 20% dimethysulfoxide (1:2, v/v), and sequenced using DYENAMIC energy transfer sequencing primers and the DYENAMIC DIRECT kit (Amersham Pharmacia Biotech) or the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Applied Biosystems).

In like manner, the polynucleotide sequences of SEQ ID NO:108-214 are used to obtain 5' regulatory sequences using the procedure above, along with oligonucleotides designed for such extension, and an appropriate genomic library.

VII. Labeling and Use of Individual Hybridization Probes

Hybridization probes derived from SEQ ID NO:108-214 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20 base pairs, is specifically described, essentially the same procedure is used with larger nucleotide fragments. Oligonucleotides are designed using state-of-the-art software such as OLIGO 4.06 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250 μCi of [γ-^{32}P] adenosine triphosphate (Amersham Pharmacia Biotech), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Pharmacia Biotech). An aliquot containing 10^7 counts per minute of the labeled probe is used in a typical membrane-based hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is carried out for 16 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature under conditions of up to, for example, 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. Hybridization patterns are visualized using autoradiography or an alternative imaging means and compared.

VIII. Microarrays

The linkage or synthesis of array elements upon a microarray can be achieved utilizing photolithography, piezoelectric printing (ink-jet printing, See, e.g., Baldeschweiler, supra), mechanical microspotting technologies, and derivatives thereof. The substrate in each of the aforementioned technologies should be uniform and solid with a non-porous surface (Schena (1999),

supra). Suggested substrates include silicon, silica, glass slides, glass chips, and silicon wafers. Alternatively, a procedure analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using thermal, UV, chemical, or mechanical bonding procedures. A typical array may be produced using available methods and machines well known to those of ordinary skill in the art and may contain any appropriate number of elements. (See, e.g., Schena, M. et al. (1995) Science 270:467-470; Shalon, D. et al. (1996) Genome Res. 6:639-645; Marshall, A. and J. Hodgson (1998) Nat. Biotechnol. 16:27-31.)

Full length cDNAs, Expressed Sequence Tags (ESTs), or fragments or oligomers thereof may comprise the elements of the microarray. Fragments or oligomers suitable for hybridization can be selected using software well known in the art such as LASERGENE software (DNASTAR). The array elements are hybridized with polynucleotides in a biological sample. The polynucleotides in the biological sample are conjugated to a fluorescent label or other molecular tag for ease of detection. After hybridization, nonhybridized nucleotides from the biological sample are removed, and a fluorescence scanner is used to detect hybridization at each array element. Alternatively, laser desorbtion and mass spectrometry may be used for detection of hybridization. The degree of complementarity and the relative abundance of each polynucleotide which hybridizes to an element on the microarray may be assessed. In one embodiment, microarray preparation and usage is described in detail below.

Tissue or Cell Sample Preparation

Total RNA is isolated from tissue samples using the guanidinium thiocyanate method and poly(A)$^+$ RNA is purified using the oligo-(dT) cellulose method. Each poly(A)$^+$ RNA sample is reverse transcribed using MMLV reverse-transcriptase, 0.05 pg/µl oligo-(dT) primer (21mer), 1X first strand buffer, 0.03 units/µl RNase inhibitor, 500 µM dATP, 500 µM dGTP, 500 µM dTTP, 40 µM dCTP, 40 µM dCTP-Cy3 (BDS) or dCTP-Cy5 (Amersham Pharmacia Biotech). The reverse transcription reaction is performed in a 25 ml volume containing 200 ng poly(A)$^+$ RNA with GEMBRIGHT kits (Incyte). Specific control poly(A)$^+$ RNAs are synthesized by in vitro transcription from non-coding yeast genomic DNA. After incubation at 37 °C for 2 hr, each reaction sample (one with Cy3 and another with Cy5 labeling) is treated with 2.5 ml of 0.5M sodium hydroxide and incubated for 20 minutes at 85 °C to the stop the reaction and degrade the RNA. Samples are purified using two successive CHROMA SPIN 30 gel filtration spin columns (CLONTECH Laboratories, Inc. (CLONTECH), Palo Alto CA) and after combining, both reaction samples are ethanol precipitated using 1 ml of glycogen (1 mg/ml), 60 ml sodium acetate, and 300 ml of 100% ethanol. The sample is then dried to completion using a SpeedVAC (Savant Instruments Inc., Holbrook NY) and resuspended in 14 µl 5X SSC/0.2% SDS.

Microarray Preparation

Sequences of the present invention are used to generate array elements. Each array element is amplified from bacterial cells containing vectors with cloned cDNA inserts. PCR amplification uses primers complementary to the vector sequences flanking the cDNA insert. Array elements are amplified in thirty cycles of PCR from an initial quantity of 1-2 ng to a final quantity greater than 5 µg. Amplified array elements are then purified using SEPHACRYL-400 (Amersham Pharmacia Biotech).

Purified array elements are immobilized on polymer-coated glass slides. Glass microscope slides (Corning) are cleaned by ultrasound in 0.1% SDS and acetone, with extensive distilled water washes between and after treatments. Glass slides are etched in 4% hydrofluoric acid (VWR Scientific Products Corporation (VWR), West Chester PA), washed extensively in distilled water, and coated with 0.05% aminopropyl silane (Sigma) in 95% ethanol. Coated slides are cured in a 110°C oven.

Array elements are applied to the coated glass substrate using a procedure described in US Patent No. 5,807,522, incorporated herein by reference. 1 µl of the array element DNA, at an average concentration of 100 ng/µl, is loaded into the open capillary printing element by a high-speed robotic apparatus. The apparatus then deposits about 5 nl of array element sample per slide.

Microarrays are UV-crosslinked using a STRATALINKER UV-crosslinker (Stratagene). Microarrays are washed at room temperature once in 0.2% SDS and three times in distilled water. Non-specific binding sites are blocked by incubation of microarrays in 0.2% casein in phosphate buffered saline (PBS) (Tropix, Inc., Bedford MA) for 30 minutes at 60 °C followed by washes in 0.2% SDS and distilled water as before.

Hybridization

Hybridization reactions contain 9 µl of sample mixture consisting of 0.2 µg each of Cy3 and Cy5 labeled cDNA synthesis products in 5X SSC, 0.2% SDS hybridization buffer. The sample mixture is heated to 65 °C for 5 minutes and is aliquoted onto the microarray surface and covered with an 1.8 cm^2 coverslip. The arrays are transferred to a waterproof chamber having a cavity just slightly larger than a microscope slide. The chamber is kept at 100% humidity internally by the addition of 140 µl of 5X SSC in a corner of the chamber. The chamber containing the arrays is incubated for about 6.5 hours at 60 °C. The arrays are washed for 10 min at 45 °C in a first wash buffer (1X SSC, 0.1% SDS), three times for 10 minutes each at 45 °C in a second wash buffer (0.1X SSC), and dried.

Detection

Reporter-labeled hybridization complexes are detected with a microscope equipped with an Innova 70 mixed gas 10 W laser (Coherent, Inc., Santa Clara CA) capable of generating spectral lines

at 488 nm for excitation of Cy3 and at 632 nm for excitation of Cy5. The excitation laser light is focused on the array using a 20X microscope objective (Nikon, Inc., Melville NY). The slide containing the array is placed on a computer-controlled X-Y stage on the microscope and raster-scanned past the objective. The 1.8 cm x 1.8 cm array used in the present example is scanned with a resolution of 20 micrometers.

In two separate scans, a mixed gas multiline laser excites the two fluorophores sequentially. Emitted light is split, based on wavelength, into two photomultiplier tube detectors (PMT R1477, Hamamatsu Photonics Systems, Bridgewater NJ) corresponding to the two fluorophores. Appropriate filters positioned between the array and the photomultiplier tubes are used to filter the signals. The emission maxima of the fluorophores used are 565 nm for Cy3 and 650 nm for Cy5. Each array is typically scanned twice, one scan per fluorophore using the appropriate filters at the laser source, although the apparatus is capable of recording the spectra from both fluorophores simultaneously.

The sensitivity of the scans is typically calibrated using the signal intensity generated by a cDNA control species added to the sample mixture at a known concentration. A specific location on the array contains a complementary DNA sequence, allowing the intensity of the signal at that location to be correlated with a weight ratio of hybridizing species of 1:100,000. When two samples from different sources (e.g., representing test and control cells), each labeled with a different fluorophore, are hybridized to a single array for the purpose of identifying genes that are differentially expressed, the calibration is done by labeling samples of the calibrating cDNA with the two fluorophores and adding identical amounts of each to the hybridization mixture.

The output of the photomultiplier tube is digitized using a 12-bit RTI-835H analog-to-digital (A/D) conversion board (Analog Devices, Inc., Norwood MA) installed in an IBM-compatible PC computer. The digitized data are displayed as an image where the signal intensity is mapped using a linear 20-color transformation to a pseudocolor scale ranging from blue (low signal) to red (high signal). The data is also analyzed quantitatively. Where two different fluorophores are excited and measured simultaneously, the data are first corrected for optical crosstalk (due to overlapping emission spectra) between the fluorophores using each fluorophore's emission spectrum.

A grid is superimposed over the fluorescence signal image such that the signal from each spot is centered in each element of the grid. The fluorescence signal within each element is then integrated to obtain a numerical value corresponding to the average intensity of the signal. The software used for signal analysis is the GEMTOOLS gene expression analysis program (Incyte).

IX. Complementary Polynucleotides

Sequences complementary to the TRFX-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring TRFX. Although use of

oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of TRFX. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the TRFX-encoding transcript.

X. Expression of TRFX

Expression and purification of TRFX is achieved using bacterial or virus-based expression systems. For expression of TRFX in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels of cDNA transcription. Examples of such promoters include, but are not limited to, the *trp-lac* (*tac*) hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the *lac* operator regulatory element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3). Antibiotic resistant bacteria express TRFX upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG). Expression of TRFX in eukaryotic cells is achieved by infecting insect or mammalian cell lines with recombinant Autographica californica nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is replaced with cDNA encoding TRFX by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription. Recombinant baculovirus is used to infect Spodoptera frugiperda (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus. (See Engelhard, E.K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945.)

In most expression systems, TRFX is synthesized as a fusion protein with, e.g., glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Pharmacia Biotech). Following purification, the GST moiety can be proteolytically cleaved from TRFX at specifically engineered sites. FLAG, an 8-amino acid peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel (1995,

supra, ch. 10 and 16). Purified TRFX obtained by these methods can be used directly in the assays shown in Examples XI and XV.

XI. Demonstration of TRFX Activity

TRFX activity is measured by its ability to stimulate transcription of a reporter gene (Liu, H.Y. et al. (1997) EMBO J. 16(17):5289-5298). The assay entails the use of a well characterized reporter gene construct, $LexA_{op}$-LacZ, that consists of LexA DNA transcriptional control elements ($LexA_{op}$) fused to sequences encoding the E. coli LacZ enzyme. The methods for constructing and expressing fusion genes, introducing them into cells, and measuring LacZ enzyme activity, are well known to those skilled in the art. Sequences encoding TRFX are cloned into a plasmid that directs the synthesis of a fusion protein, LexA-TRFX, consisting of TRFX and a DNA binding domain derived from the LexA transcription factor. The resulting plasmid, encoding a LexA-TRFX fusion protein, is introduced into yeast cells along with a plasmid containing the $LexA_{op}$-LacZ reporter gene. The amount of LacZ enzyme activity associated with LexA-TRFX transfected cells, relative to control cells, is proportional to the amount of transcription stimulated by the TRFX.

XII. Functional Assays

TRFX function is assessed by expressing the sequences encoding TRFX at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include pCMV SPORT plasmid (Life Technologies) and pCR3.1 plasmid (Invitrogen), both of which contain the cytomegalovirus promoter. 5-10 μg of recombinant vector are transiently transfected into a human cell line, for example, an endothelial or hematopoietic cell line, using either liposome formulations or electroporation. 1-2 μg of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with cell death. These events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are

discussed in Ormerod, M.G. (1994) Flow Cytometry, Oxford, New York NY.

The influence of TRFX on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding TRFX and either CD64 or CD64-GFP. CD64 and CD64-GFP are expressed on the surface of transfected cells and bind to conserved regions of human immunoglobulin G (IgG). Transfected cells are efficiently separated from nontransfected cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding TRFX and other genes of interest can be analyzed by northern analysis or microarray techniques.

XIII. Production of TRFX Specific Antibodies

TRFX substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) Methods Enzymol. 182:488-495), or other purification techniques, is used to immunize rabbits and to produce antibodies using standard protocols.

Alternatively, the TRFX amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art. (See, e.g., Ausubel, 1995, supra, ch. 11.)

Typically, oligopeptides of about 15 residues in length are synthesized using an ABI 431A peptide synthesizer (Applied Biosystems) using FMOC chemistry and coupled to KLH (Sigma-Aldrich, St. Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase immunogenicity. (See, e.g., Ausubel, 1995, supra.) Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for antipeptide and anti-TRFX activity by, for example, binding the peptide or TRFX to a substrate, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

XIV. Purification of Naturally Occurring TRFX Using Specific Antibodies

Naturally occurring or recombinant TRFX is substantially purified by immunoaffinity chromatography using antibodies specific for TRFX. An immunoaffinity column is constructed by covalently coupling anti-TRFX antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

Media containing TRFX are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of TRFX (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt

antibody/TRFX binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and TRFX is collected.

XV. Identification of Molecules Which Interact with TRFX

TRFX, or biologically active fragments thereof, are labeled with ^{125}I Bolton-Hunter reagent. (See, e.g., Bolton A.E. and W.M. Hunter (1973) Biochem. J. 133:529-539.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled TRFX, washed, and any wells with labeled TRFX complex are assayed. Data obtained using different concentrations of TRFX are used to calculate values for the number, affinity, and association of TRFX with the candidate molecules.

Alternatively, molecules interacting with TRFX are analyzed using the yeast two-hybrid system as described in Fields, S. and O. Song (1989, Nature 340:245-246), or using commercially available kits based on the two-hybrid system, such as the MATCHMAKER system (Clontech).

TRFX may also be used in the PATHCALLING process (CuraGen Corp., New Haven CT) which employs the yeast two-hybrid system in a high-throughput manner to determine all interactions between the proteins encoded by two large libraries of genes (Nandabalan, K. et al. (2000) U.S. Patent No. 6,057,101).

Various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with certain embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the following claims.

Table 1

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
1	108	095210	PITUNOT01	095210H1 (PITUNOT01), 095210R1 (PITUNOT01), 450088R1 (TLYMNOT02), 1405954F6 (LATRTUT02), 1676067F6 (BLADNOT05), 3421076H1 (UCMCNOT04), 3519949H1 (LUNGNON03), 3535670H1 (KIDNNOT25)
2	109	157953	THP1PLB02	157953F1 (THP1PLB02), 157953H1 (THP1PLB02), 279935H1 (LIVRNOT02), 293820X24 (LIVRNOT04), 1210577R7 (BRSTNOT02), 2563416H1 (ADRETUT01), 5049562H1 (BRSTNOT33), g678942
3	110	159196	ADENINB01	159196H1 (ADENINB01), 873479R1 (LUNGAST01), 1695224F6 (COLNNOT23), 4408025F6 (PROSDIT01), 4663865T6 (MEGBUNT01)
4	111	343338	THYMNOT02	343338H1 (THYMNOT02), 343338R6 (THYMNOT02), 343338T6 (THYMNOT02), 1448112F6 (PLACNOT02), 1448112R1 (PLACNOT02), 2235177X14F1 (PANCTUT02), 2235177X16F1 (PANCTUT02), 2235177X17F1 (PANCTUT02), 2241778F6 (PANCTUT02), 2241778T6 (PANCTUT02), 2729457F6 (OVARTUT05), 4053846F6 (SPLNNOT13), SBCA04252F1
5	112	402386	TMLR3DT01	402386H1 (TMLR3DT01), 402386X11 (TMLR3DT01), 568243R1 (MMLR3DT01), 568243T6 (MMLR3DT01), 731436H1 (LUNGNOT03), SAGA00508R1, SAGA00557R1
6	113	456487	KERANOT01	168091H1 (LIVRNOT01), 456487H1 (KERANOT01), 532096R1 (BRAINOT03), 619791H1 (PGANNOT01), 825933R1 (PROSNOT06), 1436382F1 (PANCNOT08), 1439054F6 (PANCNOT08), 1700156F6 (BLADTUT05), 2274307R6 (PROSNON01), 2515549H1 (LIVRTUT04), 5158675H1 (BRSTTMT02)
7	114	490256	HNT2AGT01	490256H1 (HNT2AGT01), 507309F1 (TMLR3DT02), 507309X15 (TMLR3DT02); 2724951H1 (OVARTUT05), SZZZ00188R1, SZZZ02099R1, g825070, g1242173
8	115	494740	HNT2NOT01	494740H1 (HNT2NOT01), 770196R1 (COLNCRT01), 1235126F1 (LUNGFET03), 1235126T1 (LUNGFET03), 1326711F1 (LPARNOT02), 1816820F6 (PROSNOT20), 1853059H1 (LUNGFET03)
9	116	507475	TMLR3DT02	507475H1 (TMLR3DT02), 535932R6 (ADRENOT03), 779955H1 (MYOMNOT01), 1928396T6 (BRSTNOT02), 2078558H1 (ISLTNOT01)
10	117	531581	BRAINOT03	084009X13 (HYPONOB01), 413718R1 (BRSTNOT01), 413718X22F1 (BRSTNOT01), 531581H1 (BRAINOT03), 531581T6 (BRAINOT03), 2171348H1 (ENDCNOT03), 2795710T6 (NPOLNOT01), 2926562F7 (TLYMNOT04), 2926562T7 (TLYMNOT04), 4341890H1 (BRAUNOT02), 4405904H1 (PROSDIT01)
11	118	675190	CRBLNOT01	675190H1 (CRBLNOT01), 675190X13 (CRBLNOT01), 1812672F6 (PROSTUT12), 2573205R6 (HIPOAZT01)
12	119	685434	UTRSNOT02	685434CT1 (UTRSNOT02), 685434H1 (UTRSNOT02), 1904155F6 (OVARNOT07), 2784031F6 (BRSTNOT13), 3129338F6 (LUNGTUT12)

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
13	120	788663	PROSNOT05	788663H1 (PROSNOT05), 1451931F1 (PENITUT01), 1960289H1 (BRSTNOT04), 2083142F6 (UTRSNOT08), 2542122H1 (BONRTUT01), 2581153F6 (KIDNTUT13), 3577780H1 (BRONNOT01)
14	121	870100	LUNGAST01	625091R6 (PGANNOT01), 870100H1 (LUNGAST01), 870100X12 (LUNGAST01), 1231358H1 (BRAITUT01), STEQ00206R1, SZZZ00601R1, SZZZ02045R1
15	122	879500	THYRNOT02	281880H1 (CARDNOT01), 859232R1 (BRAITUT03), 879500H1 (THYRNOT02), 1250675F6 (LUNGFET03), 1601165F6 (BLADNOT03), 1823981F6 (GBLATUT01), 2187360F6 (PROSNOT26), 2262956H1 (UTRSNOT02), 2433567H1 (BRAVUNT02), 2656846F6 (LUNGTUT09), 2993077F6 (KIDNFET02), 3085846H1 (HEAONOT03), 3181794T6 (TLYJNOT01), 4285141F6 (LIVRDIR01), 4774779H1 (BRAQNOT01), 5507484H1 (BRADDIR01), 5512965H1 (BRADDIR01), SCMA05658V1, SCMA03540V1, SCMA00007V1, g2224558
16	123	975377	MUSCNOT02	026851R1 (SPLNFET01), 786313R1 (PROSNOT05), 975377H1 (MUSCNOT02), 975377X19 (MUSCNOT02), 975377X21 (MUSCNOT02), 1354139X14 (LUNGNOT09), 2546208H1 (UTRSNOT11)
17	124	1208721	BRSTNOT02	1208721H1 (BRSTNOT02), 1286769F1 (BRAINOT11), 1456447F6 (COLNFET02), 1722840T6 (BLADNOT06), 1998475R6 (BRSTTUT03), 2740916F6 (BRSTTUT14), 3234886H1 (COLNUCT03), 4588959H1 (MASTTXT01), 4710080H1 (BRAIFET02), g1425135
18	125	1234329	LUNGFET03	259818T6 (HNT2RAT01), 264365H1 (HNT2AGT01), 349606H1 (LVENNOT01), 399059H1 (PITUNOT02), 1234329H1 (LUNGFET03), 1257012F1 (MENITUT03), 1442838F1 (THYRNOT03), 1443014R1 (THYRNOT03), 1515850F1 (PANCTUT01), 2186886F6 (PROSNOT26), 2655641F6 (THYMNOT04), 2703809F6 (OVARTUT10), g1688736, g1985577
19	126	1238747	LUNGTUT02	501158R6 (NEUTLPT01), 565047H1 (NEUTLPT01), 769541R6 (COLNCRT01), 890561T6 (STOMTUT01), 1238747H1 (LUNGTUT02), 1510233F6 (LUNGNOT14), 1510233T6 (LUNGNOT14)
20	127	1265980	BRAINOT09	1265980H1 (BRAINOT09), 2155287X13F1 (BRAINOT09), 2155287X23F1 (BRAINOT09), 2158376T6 (BRAINOT09), SAGA02430F1
21	128	1297333	BRSTNOT07	1297333H1 (BRSTNOT07), 1297333X12 (BRSTNOT07), 1297333X14 (BRSTNOT07), SAGA00259F1, SAGA00400R1

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
22	129	1312824	BLADTUT02	306400R6 (HEARNOT01), 1312824H1 (BLADTUT02), 1312824T6 (BLADTUT02), 1840110H1 (EOSITXT01), 1846489R6 (COLNNOT09), 1985201R6 (LUNGAST01), 2199162H1 (SPLNFET02), 2779784H1 (OVARTUT03), 3528903H1 (BLADNOT09), 3767951H1 (BRSTNOT24), 4251647H1 (BRADDIR01), 5205078H2 (BRAFNOT02), 5423679H1 (PROSTMT07), SANA02095F1, g1941058
23	130	1359294	LUNGNOT12	139446H1 (LIVRNOT01), 258759H1 (HNT2RAT01), 268845H1 (HNT2NOT01), 492813R1 (HNT2NOT01), 1213691H1 (BRSTTUT01), 1222480H1 (COLNTUT02), 1243093H1 (LUNGNOT03), 1319296H1 (BLADNOT04), 1359294H1 (LUNGNOT12), 1404752F6 (LATRTUT02), 1404752T6 (LATRTUT02), 1479678H1 (CORPNOT02), 1558471H1 (SPLNNOT04), 1857126H1 (PROSNOT18), 1870761H1 (SKINBIT01)
24	131	1377380	LUNGNOT10	962085R1 (BRSTTUT03), 1377380H1 (LUNGNOT10), 1670530F6 (BMARNOT03), 1853551T6 (LUNGFET03), 2119555R6 (BRSTTUT02), SCIA03178V1
25	132	1383473	BRAITUT08	780421H1 (MYOMNOT01), 1344946F6 (PROSNOT11), 1383473F6 (BRAITUT08), 1383473H1 (BRAITUT08), 1906164T6 (OVARNOT07), 2302122R6 (BRSTNOT05), 2328233R6 (COLNNOT11), 2615335F6 (GBLANOT01), 5836742H1 (BRAIDIT05)
26	133	1388860	EOSINOT01	415763R1 (BRSTNOT01), 1388860H1 (EOSINOT01), SAFC02379F1, SAFC01030F1, SAFC00771F1, SAFC02719F1
27	134	1395322	THYRNOT03	1332909F6 (PANCNOT07), 1332909X16 (PANCNOT07), 1332909X23R1 (PANCNOT07), 1332909X24R1 (PANCNOT07), 1395322H1 (THYRNOT03), 1477406F1 (CORPNOT02), 3422017H1 (UCMCNOT04)
28	135	1419370	KIDNNOT09	243596H1 (HIPONOT01), 929439R1 (CERVNOT01), 1310519F1 (COLNFET02), 1395856T1 (THYRNOT03), 1419370F1 (KIDNNOT09), 1419370H1 (KIDNNOT09), 1666159F6 (BRSTNOT09), 3461531H1 (293TF2T01), 4710948H1 (BRAIFET02), SBGA01870F1, g947108, g1991693
29	136	1429773	SINTBST01	1306171T6 (PLACNOT02), 1313558F1 (BLADTUT02), 1429773H1 (SINTBST01), 1469411F1 (PANCTUT02), 1626615F6 (COLNPOT01), 1807088F6 (SINTNOT13), 2641613F6 (LUNGTUT08), 2692245F6 (LUNGNOT23), 2695323H1 (UTRSNOT12), 2851378H1 (BRSTTUT13), 3387328F6 (LUNGTUT17)
30	137	1470820	PANCTUT02	1232690F6 (LUNGFET03), 1470820H1 (PANCTUT02), 1484705F1 (CORPNOT02), 2831707F6 (TLYMNOT03), 3073715H1 (BONEUNT01)
31	138	1483455	CORPNOT02	487811X26 (HNT2AGT01), 1483455H1 (CORPNOT02), 1849167F6 (LUNGFET03), 1856220F6 (PROSNOT18), 2822949F6 (ADRETUT06), 2822949T6 (ADRETUT06), 2851743F6 (BRSTTUT13), g2159610

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
32	139	1527064	UCMCL5T01	001612H1 (U937NOT01), 001923H1 (U937NOT01), 1235664H1 (LUNGFET03), 1412779H1 (BRAINOT12), 1527064H1 (UCMCL5T01), 1598233T6 (BLADNOT03), 1702565H1 (BLADTUT05), 1973691H1 (UCMCL5T01), 2227436H1 (SEMVNOT01), 2472092F6 (THP1NOT03), 2634126H1 (COLNTUT15)
33	140	1557491	BLADTUT04	046771H1 (CORNNOT01), 1456684F6 (COLNFET02), 1456684T6 (COLNFET02), 1554967F1 (BLADTUT04), 1557491H1 (BLADTUT04), 1992143H1 (CORPNOT02), 2687476F6 (LUNGNOT23), 3139175F6 (SMCCNOT02), 4746319H1 (SMCRUNT01)
34	141	1576862	LNODNOT03	496787F1 (HNT2NOT01), 496787R1 (HNT2NOT01), 1572855F6 (LNODNOT03), 1576862H1 (LNODNOT03), 1576862X11 (LNODNOT03), 1576862X19 (LNODNOT03), 1576862X21 (LNODNOT03), 3284579T6 (HEAONOT05), SBIA03851D1, SBIA04892D1, SBIA07089D1
35	142	1609731	COLNTUT06	112132F1 (PITUNOT01), 112132R1 (PITUNOT01), 159643X1 (ADENINB01), 1609731H1 (COLNTUT06), 1609731T6 (COLNTUT06), 5445363H1 (LNODNOT12), g2204797
36	143	1674538	BLADNOT05	1432420H1 (BEPINON01), 1579336F6 (DUODNOT01), 1674538F6 (BLADNOT05), 1674538H1 (BLADNOT05), 2656555H1 (LUNGTUT09), 4249348H1 (BRADDIR01), 4618275H1 (BRAYDIT01), 4760417H1 (BRAMNOT01), g3785154, g1623216, g899854, g1717534
37	144	1675287	BLADNOT05	868686T1 (LUNGAST01), 984876R1 (LVENNOT03), 1456253F1 (COLNFET02), 1675287H1 (BLADNOT05), 1675845H1 (BLADNOT05), 2047281F6 (THP1T7T01), 2808537H1 (BLADTUT08), 4883514F6 (LUNLTMT01)
38	145	1693903	COLNNOT23	1358877F1 (LUNGNOT09), 1573956F1 (LNODNOT03), 1693903F6 (COLNNOT23), 1693903H1 (COLNNOT23), 2184065F6 (SININOT01), 3316112F6 (PROSBPT03), SXAF02294V1
39	146	1702962	DUODNOT02	794279R6 (OVARNOT03), 814285R6 (OVARTUT01), 1702962H1 (DUODNOT02), 2186132H1 (PROSNOT26), 2880019F6 (UTRSTUT05), 5196364H1 (LUNLTUT04)
40	147	1712916	PROSNOT16	1712916F6 (PROSNOT16), 1712916H1 (PROSNOT16), 2186575F6 (PROSNOT26), g3399946
41	148	1748313	STOMTUT02	940469R6 (ADRENOT03), 1317481F6 (BLADTUT02), 1748313H1 (STOMTUT02), 1870549F6 (SKINBIT01), 2169544F6 (ENDCNOT03), 2285816H1 (BRAINON01), 2383066F6 (ISLTNOT01), 2613757F6 (ESOGTUT02), SZAS01459V1, SZAS00220V1
42	149	1754833	LIVRTUT01	710767H1 (SYNORAT04), 1396892F6 (BRAITUT08), 1754833H1 (LIVRTUT01), 1754833T6 (LIVRTUT01), 1879592F6 (LEUKNOT03), 2331424R6 (COLNNOT11), 3125146H1 (LNODNOT05), 3212201H1 (BLADNOT08), 3585117H1 (293TF4T01)

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
43	150	1798701	COLNNOT27	122777F1 (LUNGNOT01), 122777R1 (LUNGNOT01), 1215026R6 (BRSTTUT01), 1753224H1 (LIVRTUT01), 1798701H1 (COLNNOT27), 2041087H1 (HIPONON02), SAEA00596F1, SAEA00135F1
44	151	1842496	COLNNOT07	027249F1 (SPLNFET01), 1330406H1 (PANCNOT07), 1842496H1 (COLNNOT07), 1981256R6 (LUNGTUT03), 3215321F7 (TESTNOT07)
45	152	1868613	SKINBIT01	1868613H1 (SKINBIT01), 1999115R6 (BRSTTUT03), 2159835F7 (ENDCNOT02), 2453392H1 (ENDANOT01), 2753832H1 (THP1AZS08), 2781021T6 (OVARTUT03), 3597161F6 (FIBPNOT01), 4567678H1 (HELATXT01), 4998328H1 (MYEPTXT02)
46	153	1870609	SKINBIT01	474617H1 (MMLR1DT01), 1391829F6 (THYRNOT03), 1722968F6 (BLADNOT06), 1722968T6 (BLADNOT06), 1833131H1 (BRAINON01), 1870609F6 (SKINBIT01), 1870609H1 (SKINBIT01), 1870609T6 (SKINBIT01), 2542675H2 (UTRSNOT11), 2580351F6 (KIDNTUT13), 2653740H1 (THYMNOT04), 3228774H1 (COTRNOT01)
47	154	1871961	LEUKNOT02	743684F1 (BRAITUT01), 835705R1 (PROSNOT07), 1624519F6 (BRAITUT13), 1688618F6 (PROSTUT10), 1871961F6 (LEUKNOT02), 1871961H1 (LEUKNOT02), 1965802R6 (BRSTNOT04), 2453823F6 (ENDANOT01), 4689940H1 (PROSTMT05)
48	155	1876258	LEUKNOT02	808836R1 (LUNGNOT04), 1390870H1 (EOSINOT01), 1876258H1 (LEUKNOT02), SZAH00430F1, SZAH03995F1, SZAH00534F1, SZAH01526F1
49	156	1929822	COLNTUT03	040201F1 (TBLYNOT01), 424589R6 (BLADNOT01), 638245H1 (BRSTNOT03), 1251025F1 (LUNGFET03), 1391470H1 (EOSINOT01), 1699535F6 (BLADTUT05), 1929822H1 (COLNTUT03), 2218644H1 (LUNGNOT18), 2291751R6 (BRAINON01), 3242060H1 (COLAUCT01), 3317796F6 (PROSBPT03), 3401711H1 (ESOGNOT03), 3488355H1 (EPIGNOT01), 4030773H1 (BRAINOT23), 4180362H1 (SINITUT03), 4891448H1 (PROSTMT05), 5539034H1 (KIDNFEC01), g3882288
50	157	1970095	UCMCL5T01	114097F1 (TESTNOT01), 168757H1 (LIVRNOT01), 754038R1 (BRAITUT02), 772953R1 (COLNCRT01), 880261R1 (THYRNOT02), 1970095F6 (UCMCL5T01), 1970095H1 (UCMCL5T01), 2235148F6 (PANCTUT02), SAEA02374R1
51	158	1975473	PANCTUT02	1340447F1 (COLNTUT03), 1500133F6 (SINTBST01), 1663908F6 (BRSTNOT09), 1975473H1 (PANCTUT02), 3726008H1 (BRSTNOT23)
52	159	1976527	PANCTUT02	160328R6 (ADENINB01), 982222T2 (TONGTUT01), 993118R6 (COLNNOT11), 1709642T6 (PROSNOT16), 1976527F6 (PANCTUT02), 1976527H1 (PANCTUT02), 3586151F6 (293TF4T01), SXAE03918V1, SXAE05371V1
53	160	2108023	BRAITUT03	1493429H1 (PROSNON01), 2012466H1 (TESTNOT03), 2108023H1 (BRAITUT03), 2108023T6 (BRAITUT03)

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
54	161	2135746	ENDCNOT01	998857R6 (KIDNTUT01), 1384325F1 (BRAITUT08), 1727569F6 (PROSNOT14), 2135746F6 (ENDCNOT01), 2135746H1 (ENDCNOT01), 2255539R6 (OVARTUT01), 2999008H1 (OVARTUT07), 3623266H1 (ENDANOT03), 5412531H1 (BRATNOT03)
55	162	2154810	BRAINOT09	035033X11 (HUVENOB01), 035033X14 (HUVENOB01), 1857664F6 (PROSNOT18), 1857664T6 (PROSNOT18), 2154810H1 (BRAINOT09), 2847166T6 (DRGLNOT01), 5094009F6 (EPIMNON05)
56	163	2228991	PROSNOT16	2228991F6 (PROSNOT16), 2228991H1 (PROSNOT16), 3970066F6 (PROSTUT10)
57	164	2241206	PANCTUT02	1235632F6 (LUNGFET03), 1514392F1 (PANCTUT01), 1533915F1 (SPLNNOT04), 2241206H1 (PANCTUT02), 2724267X303D1 (LUNGTUT10), 5218584T6 (BRSTNOT35), 5567773H1 (TLYMNOT08)
58	165	2259590	OVARTUT01	935085T1 (CERVNOT01), 1915979H1 (PROSTUT04), 2259590H1 (OVARTUT01), 2259590R6 (OVARTUT01), 2259590T6 (OVARTUT01)
59	166	2307537	NGANNOT01	628086T6 (KIDNNOT05), 931221T6 (CERVNOT01), 2307537H1 (NGANNOT01), 2307537R6 (NGANNOT01), 2799812H1 (PENCNOT01), 3318983H1 (PROSBPT03), 4158531F6 (ADRENOT14), SBZA00461V1, SBZA04079V1
60	167	2440675	EOSITXT01	806660R6 (BSTMNOT01), 1390870H1 (EOSINOT01), 2440675H1 (EOSITXT01), SZAH00430F1, SZAH03995F1, SZAH00534F1, SZAH01526F1
61	168	2463542	THYRNOT08	2463542F6 (THYRNOT08), 2463542H1 (THYRNOT08), 2552885F6 (THYMNOT03), 2655535F7 (THYMNOT04), 2869957T6 (THYRNOT10), 3042074F7 (BRSTNOT16), 3769037H1 (BRSTNOT24), 3801333H1 (SPLNNOT12), 3927329H1 (KIDNNOT19)
62	169	2486031	CONUTUT01	1417222F6 (BRAINOT12), 2486031F6 (CONUTUT01), 2486031H1 (CONUTUT01), 2634120X315D2 (COLNTUT15), 2951631T6 (KIDNFET01), g3806506
63	170	2493052	ADRETUT05	1376888T6 (LUNGNOT10), 1488851F6 (UCMCL5T01), 2108437R6 (BRAITUT03), 2493052F7 (ADRETUT05), 2493052H1 (ADRETUT05), 2493052T6 (ADRETUT05), 2840241F6 (DRGLNOT01), 4364312H1 (SKIRNOT01)
64	171	2512074	CONUTUT01	008250X12 (HMC1NOT01), 030534X12 (THP1NOB01), 1686214F6 (PROSNOT15), 2395458F6 (THP1AZT01), 2512074H1 (CONUTUT01), 2963912F6 (SCORNOT04), 5326933F6 (DRGTNON04)
65	172	2646274	LUNGTUT11	724811R6 (SYNOOAT01), 2646274H1 (LUNGTUT11), 3436027F6 (PENCNOT05)
66	173	2672566	KIDNNOT19	1381053F1 (BRAITUT08), 2108293R6 (BRAITUT03), 2672566H1 (KIDNNOT19), 2908546F6 (THYMNOT05), 3730092H1 (SMCCNON03)
67	174	2689674	LUNGNOT23	2256960T6 (OVARTUT01), 2507571F6 (CONUTUT01), 2689674F6 (LUNGNOT23), 2689674H1 (LUNGNOT23), 2755742H1 (THP1AZS08), 5096438H1 (EPIMNON05)

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
68	175	2703282	OVARTUT10	056400H1 (FIBRNOT01), 1484887F6 (CORPNOT02), 1484887T6 (CORPNOT02), 1641813F6 (HEARFET01), 1810188H1 (PROSTUT12), 2351291F6 (COLSUCT01), 2703282H1 (OVARTUT10), 3790456H1 (BRSTNOT28), 4084543T6 (CONFNOT02), 4994160H1 (LIVRTUT11), 5393763H1 (KIDNNOT32)
69	176	2738293	OVARNOT09	412176R1 (BRSTNOT01), 418633T6 (BRSTNOT01), 1232594F1 (LUNGFET03), 1301651T6 (BRSTNOT07), 2738293F6 (OVARNOT09), 2738293H1 (OVARNOT09), 5290883H1 (LIVRTUS02)
70	177	2772776	PANCNOT15	784334R1 (PROSNOT05), 2772776H1 (PANCNOT15), 3750404H1 (UTRSNOT18)
71	178	2774476	PANCNOT15	2774476H1 (PANCNOT15), 3664676T6 (PANCNOT16), 3835889F6 (PANCNOT17), 4167883X305V1 (PANCNOT21), SCCA02152V1
72	179	2804624	BLADTUT08	162435R1 (ADENINB01), 1304830T1 (PLACNOT02), 2080378X19F1 (UTRSNOT08), 2660596H1 (LUNGTUT09), 2804624H1 (BLADTUT08)
73	180	2848225	BRSTTUT13	346073X101 (THYMNOT02), 346073X26C1 (THYMNOT02), 391609T6 (TMLR2DT01), 2848225H1 (BRSTTUT13), 4624612T6 (ENDVNOT01)
74	181	2882241	UTRSTUT05	1637060F6 (UTRSNOT06), 1711682F6 (PROSNOT16), 1902475H1 (OVARNOT07), 2017387F6 (THP1NOT01), 2882241F6 (UTRSTUT05), 2882241H1 (UTRSTUT05), 3532864H1 (KIDNNOT25)
75	182	2939011	THYMFET02	897237R1 (BRSTNOT05), 897237T1 (BRSTNOT05), 1618381F6 (BRAITUT12), 2679105F6 (SINIUCT01), 2939011F6 (THYMFET02), 2939011H1 (THYMFET02), 2939011T6 (THYMFET02)
76	183	2947188	BRAITUT23	377292X1 (NEUTFMT01), 425953R6 (BLADNOT01), 425953T6 (BLADNOT01), 425953X28 (BLADNOT01), 429350T6 (BLADNOT01), 451192F1 (TLYMNOT02), 451192R1 (TLYMNOT02), 1786579H1 (BRAINOT10), 2947188H1 (BRAITUT23)
77	184	3094001	BRSTNOT19	1494663T6 (PROSNON01), 2083139X11F1 (UTRSNOT08), 3094001H1 (BRSTNOT19)
78	185	3110061	BRSTTUT15	986428R6 (LVENNOT03), 1449222R1 (PLACNOT02), 3085841F6 (HEAONOT03), 3110061F7 (BRSTTUT15), 3110061H1 (BRSTTUT15), 4308349T6 (BRAUNOT01), 4637040F6 (MYEPTXT01)
79	186	3146614	PENCNOT06	638370R1 (BRSTNOT03), 1398786T1 (BRAITUT08), 1435622F1 (PANCNOT08), 1720684F6 (BLADNOT06), 2194122F6 (THYRTUT03), 2459594H1 (THYRNOT08), 3146614H1 (PENCNOT06), 3278069H1 (STOMFET02), 3357696F6 (PROSTUT16)
80	187	3295381	TLYJINT01	2222227F6 (LUNGNOT18), 3295381H1 (TLYJINT01), SZZZ00995R1, SZZZ00226R1, SZZZ00209R1, SZZZ00347R1, SZZZ00451R1

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
81	188	3364774	PROSBPT02	1339847F6 (COLNTUT03), 1415866F6 (BRAINOT12), 2458556T6 (ENDANOT01), 2515467F6 (LIVRTUT04), 2523246H1 (BRAITUT21), 3095773H1 (CERVNOT03), 3315208F6 (293TF2T01), 3364774H1 (PROSBPT02), 3697590H1 (SININOT05), 4618612H1 (BRAYDIT01), g1422476
82	189	3397777	UTRSNOT16	2906192F6 (THYMNOT05), 3046506F7 (HEAANOT01), 3046506X329D1 (HEAANOT01), 3046506X331D1 (HEAANOT01), 3397777F7 (UTRSNOT16), 3397777H1 (UTRSNOT16), 3846636H1 (DENDNOT01), 4569754H2 (PROSTUT21)
83	190	3403046	ESOGNOT03	2754425R6 (THP1AZS08), 3403046H1 (ESOGNOT03), 3844619F6 (DENDNOT01)
84	191	3538506	SEMVNOT04	483831H1 (HNT2RAT01), 1451166F1 (PENITUT01), 3187785H1 (THYMNON04), 3538506F6 (SEMVNOT04), 3538506H1 (SEMVNOT04), 3868721F6 (BMARNOT03), 5108547F6 (PROSTUS19), 5163595H1 (ENDIUNT01), 5324664H1 (FIBPFEN06), g2056736
85	192	3575519	BRONNOT01	970343R6 (MUSCNOT02), 975169R6 (MUSCNOT02), 3575519H1 (BRONNOT01), SCSA04735V1, SCSA03846V1
86	193	3598694	FIBPNOT01	1330295F1 (PANCNOT07), 3332508T6 (BRAIFET01), 3520552H1 (LUNGNON03), 3598694H1 (FIBPNOT01), 5203510H1 (STOMNOT08), 5506937H1 (BRADDIR01), SCCA00526V1, SCCA04468V1, SCCA03065V1, SCCA02377V1, SCCA00888V1, SCCA02832V1
87	194	3638819	LUNGNOT30	837827X22 (PROSNOT07), 837827X23 (PROSNOT07), 3638819H1 (LUNGNOT30)
88	195	3717139	PENCNOT10	3717139H1 (PENCNOT10), g2106014, g2980871
89	196	3892962	BRSTTUT16	594617R6 (BRAVUNT02), 837890X18 (PROSNOT07), 1961640R6 (BRSTNOT04), 2330093H1 (COLNNOT11), 2726737F6 (OVARTUT05), 3892962H1 (BRSTTUT16)
90	197	4153521	MUSLTMT01	118141F1 (MUSCNOT01), 487811X24 (HNT2AGT01), 487811X26 (HNT2AGT01), 868070R6 (BRAITUT03), 1832527T6 (BRAINON01), 2851743T6 (BRSTTUT13), 4153521H1 (MUSLTMT01), 4531734H1 (PROSTMT03), SZZZ01004R1
91	198	4585038	OVARNOT13	546958R6 (BEPINOT01), 656154H1 (EOSINOT03), 3415219H1 (PTHYNOT04), 3683524H1 (HEAANOT01), 3750253H1 (UTRSNOT18), 4089875H1 (LIVRNOT06), 4585038H1 (OVARNOT13), g756767, g756768
92	199	4674640	NOSEDIT02	191268R1 (SYNORAB01), 1414304F6 (BRAINOT12), 3272067F6 (BRAINOT20), 4674640H1 (NOSEDIT02), SCDA05786V1, SCDA07745V1, SZAP01877V1
93	200	4676066	NOSEDIT02	875407R1 (LUNGAST01), 1478971F6 (CORPNOT02), 1749564F6 (STOMTUT02), 2263128H1 (UTRSNOT02), 4676066H1 (NOSEDIT02), 5449856H1 (BSCNDIT02), 5487675H1 (DRGTNON04), g3118452
94	201	4830687	BRAVTXT03	534025F1 (BRAINOT03), 4830687H1 (BRAVTXT03)

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
95	202	4880891	UTRMTMT01	055751H1 (FIBRNOT01), 1288342F6 (BRAINOT11), 1288342T6 (BRAINOT11), 1396095F6 (THYRNOT03), 1820602F6 (GBLATUT01), 2123331F6 (BRSTNOT07), 2462011F6 (THYRNOT08), 2645166X303D1 (OVARTUT03), 2666343H1 (ADRETUT06), 2666343T6 (ADRETUT06), 2715208F6 (THYRNOT09), 2881019F6 (UTRSTUT05), 3448078X331D1 (UTRSNON03), 4880891H1 (UTRMTMT01), 5465061H1 (LNODNOT11), 5503746H1 (BRABDIR01), SBLA03155F1, SBLA02267F1
96	203	4909754	THYMDIT01	014580H1 (THP1PLB01), 1348640F6 (PROSNOT11), 1685157F6 (PROSNOT15), 3427741H1 (BRSTNOR01), 3540578H1 (SEMVNOT04), 4909754F6 (THYMDIT01), 4909754H1 (THYMDIT01), 5834707H1 (BRAIDIT05), g1940399
97	204	4911931	THYMDIT01	428504F1 (BLADNOT01), 468041R6 (LATRNOT01), 2342984F6 (TESTTUT02), 2887138H1 (SINJNOT02), 4911931H1 (THYMDIT01)
98	205	4920433	TESTNOT11	2006765R6 (TESTNOT03), 4920433F6 (TESTNOT11), 4920433H1 (TESTNOT11)
99	206	5042113	COLHTUT01	537782R6 (LNODNOT02), 537782T6 (LNODNOT02), 724003H1 (SYNOOAT01), 2700935X302B2 (OVARTUT10), 2700935X302F1 (OVARTUT10), 3572973T6 (BRONNOT01), 5042113H1 (COLHTUT01), SBIA02608D1, SBIA08390D1
100	207	5083853	LNOGTUT01	1537455H1 (SINTTUT01), 5083853F6 (LNOGTUT01), 5083853H1 (LNOGTUT01), 5083853T6 (LNOGTUT01)
101	208	5283981	TESTNON04	542319F1 (OVARNOT02), 542319X15F1 (OVARNOT02), 542319X17F1 (OVARNOT02), 1710519F6 (PROSNOT16), 5283981H1 (TESTNON04)
102	209	5510549	BRADDIR01	1257226F6 (MENITUT03), 1654887F6 (PROSTUT08), 1866033F6 (PROSNOT19), 2309180H1 (NGANNOT01), 2516285F6 (LIVRTUT04), 3558606H1 (LUNGNOT31), 4689374H1 (LIVRTUT11), 5510549H1 (BRADDIR01)
103	210	5544862	TESTNOC01	1210853R1 (BRSTNOT02), 1803417F6 (SINTNOT13), 5544862F6 (TESTNOC01), 5544862H1 (TESTNOC01), 5544862T6 (TESTNOC01), 5547247F6 (TESTNOC01), g989649, g3246546, g2112974, g697810
104	211	5573394	TLYMNOT08	027981H1 (SPLNFET01), 310525T6 (TMLR2DT01), 826528R1 (PROSNOT06), 868061R6 (BRAITUT03), 1985188T6 (LUNGAST01), 2207165F6 (SINTFET03), 5507004H1 (BRADDIR01), 5573394H1 (TLYMNOT08), SBIA11388D1, SBIA11986D1, SBIA03475D1
105	212	5850840	FIBAUNT02	232422F1 (SINTNOT02), 232442R1 (SINTNOT02), 826837R1 (PROSNOT06), 1286853F1 (BRAINOT11), 2058494R6 (OVARNOT03), 2842471F6 (DRGLNOT01), 3105825F6 (BRSTTUT15), 3617707H1 (EPIPNOT01), 3620903H1 (BRSTNOT25), 4148432H1 (SINITUT04), 5850840H1 (FIBAUNT02)
106	213	5942936	COLADIT05	121785R6 (MUSCNOT01), 797379T6 (OVARNOT03), 797379X14R1 (OVARNOT03), 797379X25R1 (OVARNOT03), 3690756H1 (HEAANOT01), 5942936H1 (COLADIT05)

Table 1 (cont.)

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
107	214	5951431	LIVRTUN04	623984R6 (PGANNOT01), 676513T6 (CRBLNOT01), 1730442F6 (BRSTTUT08), 2640175F6 (LUNGTUT08), 3360767F6 (PROSTUT16), 5951431H1 (LIVRTUN04), SAEA03186R1

Table 2

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
1	095210	463	S72 T7 S16 S49 T371 T58 S68 S72	N38 N53	ATP/GTP-binding site motif A (P-loop): G412-S419 Zinc finger C2H2 type domain: C133-H153 C161-H181 C189-H209 C217-H237 C245-H265 C273-H293 C301-H321 C329-H349 C357-H377 C385-H405 C413-H423 C441-H461 KRAB box domain: V6-R66	g498721 zinc finger protein [Homo sapiens] Abrink, M. et al. (1995) DNA Cell Biol. 14:125-136	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_BLOCKS BLIMPS_PRODOM BLAST_DOMO
2	157953	216	T28 T140 T2 T139 S210	N152	bZIP transcription factors basic domain signature: K147-R163	g4996451 leucine-zipper protein	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_BLOCKS BLAST_DOMO
3	159196	284	S153 S44 T189 T232 S3 T62 S125 S148 T245 Y140 Y196	N94 N95 N207	Zinc finger C2H2 type domain: C86-H106 C114-H134 C142-H162 C170-H190 C198-H218 C226-H246 C254-H274	g55471 Zinc finger protein expressed in post-meiotic spermatogenesis Denny, P. and Ashworth, A. (1991) Gene 106:221-227	MOTIFS BLAST_GENBANK BLAST_PFAM

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
4	343338	1416	S817 T406 S142 S236 S272 S329 S395 S412 S413 T426 S427 S439 S474 S475 S476 T531 S669 S711 T735 T832 S876 S878 T954 T960 S972 S1051 T1138 S1378 T42 S141 T262 T307 S315 T336 T345 S381 T400 T469 S482 S506 T625 T634 T707 T803 S843 S869 S891 T892 S993 S1002 T1033 S1103 T31 S1143 S1169 T1317 S1329 S1336 S1397 Y658 T1406 Y346 Y813 Y945 Y970	N40 N261 N409 N467 N1040 N1130 N1167	ATP/GTP-binding site motif A (P-loop): A1086-T1093 A1131-T1138 Beta-transducin family Trp-Asp repeats signature: V34-S48 L77-L91 Bromodomain signature: A778-H853, P935-T991	g7717364 homolog to cAMP response element binding and beta transducin family proteins [Homo sapiens]	MOTIFS BLAST_GENBANK BLAST_PFAM PROFILESCAN BLIMPS_PRINTS BLAST_PRODOM BLAST_DOMO
5	402386	426	S292 T14 S65 S115 S24 T36 T139 T164 T192 S196 S380 Y229	N12	Zinc finger C2H2 type domain: F6-G44, C102-H124, Y169-H191, C171-H191, Y225-H247, Y253-H276, H282-H304, Y310-H332, Y338-H360, Y366-H388 KRAB box domain: V4-V67	g487785 zinc finger protein ZNF136 Tommerup, N. and Vissing, H. (1995) Genomics 27:259-264	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS-PRODOM BLAST_PRODOM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
6	456487	686	S407 T408 S27 S94 S117 T176 S185 T224 S225 S260 S318 T426 T427 S460 S542 S558 T559 S569 T595 S611 T618 S668 T6 T135 S247 S256 S278 S293 T299 T337 S357 S386 S451 S555	N79 N128 N213 N616	Putative GTPase activating protein for Arf: A464-E584 HIV REV interacting protein: N476-R512, V516-N537 Zinc finger motif: Q468-P581	g3880859 similar to Ank repeat (2 domains)	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_PRINTS BLAST_PRODOM BLAST_DOMO
7	490256	348	T3 T108 T114 T163 T181 S29 S134 S302		Zinc finger C2H2 type domain: C238-H258 C266-H286 C294-H314 C322-H342 Zinc finger motif: E8-Q173	g2316003 zinc finger protein [Homo sapiens] Lee, P.L. et al. (1997) Genomics 43:191-201	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_DOMO
8	494740	181	T22 T37 S60 T78 T87 S12 T70 T124 S157		Zinc finger motif: F79-G117 KRAB box: V77-R126	g487836 transcription factor	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
9	507475	126	S2 S15 S71 S104 Y97		TFIIS zinc ribbon domain signature: G65-K123	g7212805 transcription-associated zinc ribbon protein [Homo sapiens] Fan, W. et al. (2000) Genomics 63:139-141	MOTIFS BLAST_GENBANK PROFILESCAN BLIMPS_BLOCKS BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
10	531581	610	S177 S410 T438 T466 S44 S55 S125 T146 S233 S239 S282 S289 S482 S507 S523 S531 S532 T537 S539 T179 S188 T255 S279 S316 S462 Y81 Y415 Y443 Y471	N194 N206	Zinc finger C2H2 type domain: C304-H324 C332-H352 C360-H381 C389-H409 C417-H437 C445-H465 C473-H493 C501-H522 Zinc finger activator domain: M9-E124	g8843908 zinc finger protein SBBIZ1 [Homo sapiens]	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
11	675190	111	T102 S17 S24 T33 T67 S9 S43 S97	N3	Zinc finger protein domain: F25-G63 KRAB box domain: S22-P94	g10442700 zinc-finger protein ZBRK1 [Homo sapiens] Zheng L. et al. (2000) Mol Cell 6:757-768	MOTIFS BLAST_GENBANK BLIMPS_PRODOM BLAST_DOMO BLAST_PFAM
12	685434	152	T6 T17 S109	N15		g4336830 RFX-Bdelta4 immunodeficiency-associated transcription factor Nagarajan, U.M. et al. (1999) Immunity 10:153-162	MOTIFS BLAST_GENBANK
13	788663	131	S30 S65 T73 S124 T45 S60 S65	N122	Transcription factor domain: R15-K96	G2583171 CCAAT-binding transcription factor subunit AAB-1 Chen, H. et al. (1998) Genetics 148:123-130	MOTIFS BLAST_GENBANK BLAST_DOMO
14	870100	541	S7 S24 S69 S85 S99 S253 T255 T302 S505 S151 T245 T315 S356 S521	N192 N450 N454	Zinc finger C2H2 type domain: C152-H172, C180-H200, C208-H228, C362-H382, C390-H410, C418-H438, C446-H466, C474-H494	g189044 zinc finger protein 42 (MZF-1, preferentially expressed in myeloma cells) Hromas, R. et al. (1991) J Biol Chem 266:14183-14187	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
15	879500	1828	S1194 S1283 S1307 S1390 S1395 S1467 S1530 S1554 S1614 S1629 S1651 S1652 S1653 S1717 S1766 S1770 S1775 S1820 S323 S443 S487 S497 S691 S716 S767 S822 S894 S921 S926 S980 S994 T1271 T1322 T1333 T1354 T1482 T1712 T1731 T1784 T322 T451 T549 T692 T727 T770 T803 T908 T976	N174 N725 N794 N1197	Helicases conserved c-terminal domain: D672-G755	g5106572 transcriptional activator SRCAP Johnston, H. et al. (1999) J Biol Chem 274:16370-16376	MOTIFS BLAST_GENBANK HMMER_PFAM BLAST_PRODOM BLAST_DOMO
16	975377	482	S185 S200 S258 S295 S319 S330 S366 S408 S463 T118 T123 T196 T205 T209 T461 T60 Y230 Y77	N306	Zinc finger C3HC4 type signature: K57-L112, I208-C236, C305-I314	g1304599 ZNF127-Xp (associated with Prader-Willi behavioral syndrome) Jong, M.T. et al. (1999) Hum Mol Genet 8:783-793	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_BLOCKS
17	1208721	264	S11 S59 T100 T114 T235 S259 S23 S138				MOTIFS
18	1234329	350	S170 S229 T290 S303 S129 S235 T331		Zinc finger C3HC4 type signature: C298-C338 PHD-finger: R313-Q327	g3880441 similar to zinc finger C3HC4 type	MOTIFS BLAST_GENBANK HMMER_PFAM PROFILESCAN BLIMPS_PFAM

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
19	1238747	549	S102 S175 S248 S273 S296 S303 S329 S346 S364 S437 S438 S485 T201 T271 T287 T370 T375 T396 T44 T467 T498 T524 T70	N77 N328	SAND DNA-binding domain: S454-L535	g9964115 transcriptional coactivator Sp110 [Homo sapiens] Bloch, D.B. et al. (2000) Mol Cell Biol 20:6138-6146	MOTIFS BLAST_GENBANK HMMER_PFAM
20	1265980	337	S22 T84 T85 T56 S131 S238 S242 T247 T326 S47 T56 T127 T135 S230 S272 Y281		Helix-loop-helix DNA binding domain: R95-S147, M1-L73 Myc-type 'helix-loop-helix' dimerization domain signature: E103-R118, T127-S147, N111-N164, E66-Q171 Transcription regulation domain: R191-N337	g4566748 basic helix-loop-helix transcription factor Ndr1 Liao, J. et al. (1999) DNA Cell Biol 18:333-344	MOTIFS BLAST_GENBANK HMMER_PFAM PROFILESCAN BLIMPS_BLOCKS BLAST_PRODOM BLAST_DOMO
21	1297333	581	S16 S29 T41 S47 T35 S92 S110 T184 S254 T368 S480 S493 S531 Y56 Y89	N78 N90 N201 N426	Zinc finger C2H2 type domain: C135-H155 C163-H183 C191-H212, C220-H240, C248-H268, C276-H296 C304-H324 C332-H352 C360-H380, C388-H408, C416-H436, C444-H464, C472-H492, C500-H520	g387079 zinc finger protein (mkr5) Chowdhury, K. et al. (1988) Nucleic Acids Res 16:9995-10011	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
22	1312824	591	S126 S127 S167 S278 S293 S389 S404 S435 S460 S510 S546 S64 S88 T203 T298 T377 T554 Y233	N296 N384 N489	Ets-related transcription factor domain: D273-F591, I180-F261 I180-K193, E206-K224, H225-Y243, Y244-K262	g972940 Elf-1 Transcription regulation protein Davis, J.N. and Roussel, M.F. (1996) Gene 171:265-269	MOTIFS BLAST_GENBANK HMMER_PFAM PROFILESCAN BLIMPS_BLOCKS BLIMPS_PRINTS BLAST_PRODOM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
23	1359294	767	S141 S391 S43 S461 S463 S485 S567 S620 S664 S75 T111 T201 T278 T291 T301 T494 T580 T646 T696 T730 T79	N18 N288 N549 N728	'Cold-shock' DNA-binding domain signature: Y37-V88, L121-M146, F166-R215 F329-V365, F499-N549, F654-W705 Unr protein DNA binding repeat domain: E98-D767	g57455 unr protein Ferrer, N. et al. (1999) DNA Cell Biol 18:209-218	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLAST_PRODOM BLAST_DOMO
24	1377380	206	S11 S131 S15 S152 S163 S167 S181 S193 S2 S34 S38 S84 S85 S93 T51			g7012714 L2DTL WD-40 repeat protein [Homo sapiens]	MOTIFS BLAST_GENBANK
25	1383473	352	S74 T95 T154 S165 S222 S322 S207 S236 S297 S308	N104 N205	Signal peptide motif: M1-A23 Transmembrane motif: L243-L259, C302-C339 Baculovirus inhibitor of apoptosis protein repeat (BIR): L298-C336	g4587558 Similar to X-linked apoptosis inhibitor	MOTIFS BLAST_GENBANK HMMER
26	1388860	532	S153 S27 S409 S465 S520 T103 T17 T360 T39 T49 Y138 Y367	N42 N65	Zinc finger C2H2 type domain: C201-H221 C229-H249 C257-H277 C285-H305 C313-H333 C341-H361 C369-H389 C397-H417 C425-H445, C453-H473, C481-H500, C508-H528 Zinc finger domain: F9-G47, K48-K146 KRAB box domain: D5-E78	g4519270 Kruppel-type zinc finger protein Katoh, O. (1998) Biochem. Biophys. Res. Commun. 249:595-600	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
27	1395322	444	S105 S134 S155 S319 S375 T110 T291 T347 T378 T69 T7 T88 Y40	N54 N153 N166 N287	Zinc finger C2H2 type domain: C283-H303, C311-H331, C339-H359 C367-H387 C420-H440	g6063139 POZ/zinc finger transcription factor ODA-8 [Mus musculus]	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
28	1419370	347	S183 T307 T14 T263 T300		Zinc finger C3HC4 type signature: C164-C202	g11611473 Deltex3 Kishi, N. et al. (2001) Int. J. Dev. Neurosci. 19:21-35	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS PROFILESCAN
29	1429773	308	S29 S31 T250 S257 Y130	N112	Transmembrane domain: P213-M237	g7542723 DHHC1 protein [Homo sapiens]	MOTIFS BLAST_GENBANK HMMER
30	1470820	80	S14 S32 T21 S36 S72 Y63		GC-rich sequence DNA binding factor domain: R11-V75 (P-value = 5.9 x 10^{-6}		MOTIFS
31	1483455	570	S116 S132 S181 S211 S470 S564 S70 S79 S87 T14 T143 T168 T237 T5 T54 T569 T88	N212 N502 N530	ATP/GTP-binding site motif A (P-loop) A216-S223 Zinc finger C2H2 type domain C238-H258, C266-H286, C294-H314, C322-H342, C350-H370, C378-H398, C406-H426, C434-H454, C462-H482, C490-H510, C518-H538 Zinc finger protein motif: V4-W77 KRAB box domain: V4-M73	g7688669 zinc finger protein ZNF140-like protein [Homo sapiens]	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
32	1527064	390	S107 S145 S167 S344 S354 S52 T112 T162 T172 T219 T352	N160 N214	Transcription factor domain: V102-E371 Heat shock factor (transcriptional activator) signature: L317-I329	g 532313 NF45 protein Kao, P.N. et al. (1994) J Biol Chem 1994 Aug 12;269:20691-9	MOTIFS BLAST_GENBANK BLIMPS_PRINTS BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
33	1557491	601	S158 S163 S179 S219 S313 S334 S355 S513 S559 S82 T186 T187 T190 T218 T246 T318 T412 T430 T482 T486 T514 T594 Y75	N2 N104 N484	Zinc finger C2H2 type domain C418-H438, C446-H466, C474-H494, C502-H522, C533-H553	g 220643 zinc finger protein	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS-PRODOM
34	1576862	834	S127 S135 S36 S50 S520 S531 S628 S679 S696 S70 S745 S798 S803 S805 S9 T391 T445 T487 T543 T663 T688 T724 T761 T791		PHD finger: C219-I233 Zinc finger protein motif: C202-R260, L256-H364 Peregrin transcriptional regulator domain: D199-K389, A524-A551	g1510153 similar to human bromodomain protein BR140 Nagase, T. et al. DNA Res 1996 Oct 31;3(5):321-9, 341-54	MOTIFS BLAST_GENBANK BLIMPS_PFAM BLAST_PRODOM BLAST_DOMO
35	1609731	499	S104 S108 S16 S50 S56 S81 T155 T259 T7 Y134	N139	Zinc finger C2H2 type domain: C169-H189, C197-H217, C225-H245, C253-H273, C281-H301, C309-H329, C337-H358, C365-H385, C393-H413, C421-H441, C449-H469, C477-H497 KRAB box domain: Q3-V71	g456269 zinc finger protein 30 Denny, P. and Ashworth, A. (1994) Mamm. Genome 5:643-645	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
36	1674538	402	S102 S158 S193 S219 S324 S384 T12 T292 T3 T344 T354 Y351	N303 N382	Zinc finger C2H2 type domain: C73-H93, C101-H121, C129-H149, C157-H177, C185-H205, C213-H233, C241-H261, C269-H289 Zinc finger protein domain: E62-H121, Q82-K153, K162-K237, K246-K319	g 55473 zinc finger protein	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLAST_PRODOM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
37	1675287	579	S134 S22 S270 S347 S57 T176 T222 T293 T526 T535 T537 T82 Y285 Y362		Zinc finger C3HC4 type signature: C400-C408 Zinc finger protein domain: C206-C408	g1136384 C3HC4 containing protein	MOTIFS BLAST_GENBANK BLIMPS_BLOCKS BLAST_PRODOM
38	1693903	426	S12 S231 S290 S328 S360 S381 S63 T114 T318 T408	N246	CCCH-Zinc finger protein motif: C113-H123		MOTIFS BLIMPS-PFAM
39	1702962	266	S78 T127 T163 T171 T196 T261 Y203	N20	Zinc finger C2H2 type domain: F175-H197, H193-C205, E194-H221, C205-H225, H225-H249, P230-S243, F231-H253	g5001720 odd-skipped related 1 protein [Mus musculus] So, P.L. and Danielian, P.S. (1999) Mech. Dev. 84:157-160	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_DOMO
40	1712916	358	S160 S164 S21 S230 S255 S267 S269 S286 S291 S299 S350 T101 T131 T99 Y97	N228 N238 N249 N284	'Homeobox' domain signature: K74-K129, N95-L106, L106-K129, S110-K129	g 1899230 iroquois-class homeodomain protein IRX-2a	MOTIFS BLAST_GENBANK BLIMPS_BLOCKS BLIMPS_PRINTS BLAST_DOMO
41	1748313	260	S102 S183 S204 S228 S35 S74 T13 T145 T167 T176 T30	N53 N124 N178			MOTIFS
42	1754833	263	S109 S177 S45 S83 S95 T31 T55 T59 T67 T74	N258	Zinc finger C3HC4 type signature: C181-C221, S177-T232	g3790583 RING-H2 finger protein RHC1a	MOTIFS BLAST_GENBANK HMMER_PFAM PROFILESCAN
43	1798701	581	S356 S368 S43 S473 S8 T145 T166 T202 T309 T360 T377 T425 T486 T556 T559 T56 T95 Y175	N77 N164 N550		g6688742 putative TH1 protein [Mus musculus]	MOTIFS BLAST_GENBANK
44	1842496	117	S4			g 4336506 transcription elongation factor	MOTIFS BLAST_GENBANK

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
45	1868613	202				g171091 ASF1 [Saccharomyces cerevisiae] DNA repair-associated protein Le, S. et al. (1997) Yeast 13:1029-1042	MOTIFS BLAST_GENBANK BLAST_PRODOM
46	1870609	442	S166 S18 S308 S315 S322 S341 S358 S373 S400 S401 T129 T176 T26 T303 T333 T422	N398	Zinc finger C3HC4 type signature: C140-C177	g5931953 autocrine motility factor receptor [Mus musculus] Shimizu, K. et al. (1999) FEBS Lett. 456:295-300	MOTIFS BLAST_GENBANK BLAST_PFAM
47	1871961	765	S177 S198 S264 S514 S547 S604 S682 T225 T269 T349 T504 T645 T696	N81 N175 N520	Zinc finger C2H2 type domain: C595-H617, C687-H709 GAL 11 transcription factor motif: T347-M627 Coiled coil domain: Q4-Q44, E206-Q428	g6672074 nuclear protein NP94 [Homo sapiens]	MOTIFS BLAST_GENBANK
48	1876258	352	S118 S153 S222 S255 S317 S9 T250 T289 T321		ATP/GTP-binding site motif A (P-loop): A193-T200 Zinc finger C2H2 type domain: C165-H186, C168-S222, C194-H214, C244-H264, C247-Q301, C272-H292, C275-E329, P297-S310, C300-H320, L313-G322, H316-C328, C328-H349, F323-K352	g 4165083 growth factor independence-1B (transcription factor expressed in t-lymphocytes) B. Rodel et al. Genomics 1998 Dec 15;54(3):580-2	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
49	1929822	1102	S1001 S1008 S1051 S1067 S11 S346 S365 S425 S740 S805 S82 S874 S891 S921 S934 S953 S955 S970 S982 T142 T171 T18 T443 T488 T51 T52 T520 T661 T782 T995 Y764 Y818	N50 N132 N315 N398 N439 N486 N674 N857 N887 N951 N1030 N1049 N1066 N1079	Homeobox domain: L771-R813 Zinc finger C2H2 type domain: C514-H536 Glutaredoxin active site: C514-V524	g4406073 activity-dependent neuroprotective protein (contains a glutaredoxin active site) Bassan, M. J Neurochem 1999 Mar;72(3):1283-93	MOTIFS BLAST_GENBANK BLIMPS_BLOCKS
50	1970095	121	T25 S32 T39 T63 S72 S91	N26		g5713279 Yippee protein [Drosophila melanogaster]	MOTIFS BLAST_GENBANK
51	1975473	233	T34 S8 S25 S65 T174 S199	N26	Signal peptide: M1-A62 Myc-type 'helix-loop-helix' dimerization domain signature: L7-T63, V11-P122, R31-Q85, E39-H54, S65-Q85 FOS-type leucine zipper: L84-L105	g4704419 WS basic-helix-loop-helix leucine zipper protein [Homo sapiens] Meng, X. et al. (1998) Human Genetics 103:590-599	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLAST_DOMO
52	1976527	147	T63 S71 T114 S122	N28 N65	Signal peptide: M1-A52 NFYB transcription factor subunit: R4-K100, P5-R94, K20-M76 CCAAT-binding transcription factor motif: A56-R93, E6-D111	g9623363 DNA polymerase epsilon p17 subunit [Homo sapiens] Li, Y. et al. (2000) J. Biol. Chem. 275:23247-23252	MOTIFS BLAST_GENBANK PROFILESCAN BLIMPS_BLOCKS BLIMPS_PRINTS BLAST_PRODOM BLAST_DOMO
53	2108023	96	T32 T7 S13 T50 T56 S73	N36		g9294739 bithoraxoid-like protein [Homo sapiens]	MOTIFS BLAST_GENBANK

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
54	2135746	259	S56 S120 S166 S181 S233 S23 S29 S89 T208		Signal peptide: M1-G20		MOTIFS SPSCAN
55	2154810	474	S88 S156 S50 S56 T80 T84 T124 S140 S145 Y94	N38 N97	Zinc finger C2H2 type domain: C172-H192, C200-H220, C228-H248, C256-H276, C284-H304, C312-H332, C340-H360, C368-H388, C396-H416 Zinc finger protein motif: F8-G46 KRAB box domain: S5-Y75	g456269 zinc finger protein 30	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
56	2228991	231	T167 S213 T99 S186 T223 S10 S35 S67 T99	N97	Signal peptide: M1-I29 Prenyl group binding site (CAAX box) T228-D231 Zinc finger domain: C166-H176		MOTIFS SPSCAN BLIMPS_PFAM
57	2241206	456	S37 S404 S406 T183 T205 T212 T264 T295 T300 T352 T50 T72	N430	RNA-binding RGG-box domain I392-G452	g 1177636 transcriptional activator SPO8	MOTIFS BLAST_GENBANK BLAST_DOMO
58	2259590	159	S87 T96 S11 S24 S25 T118 T146		Zinc finger protein motif: F88-G126 KRAB box domain: V86-C156	g506502 NK10 Zinc finger repressor protein [Mus musculus] 2.9e-15 47%ID aa 75-159 Lange, R. et al. DNA Cell Biol 1995 Nov;14(11):971-81	MOTIFS BLAST_GENBANK BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
59	2307537	260	T66 S124 S182 S197 T7 S56 S77	N36 N195		g4325209 endocrine regulator	MOTIFS BLAST_GENBANK

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
60	2440675	352	S118 S153 S222 S255 S317 S9 T250 T289 T321		A193 ATP/GTP-binding site motif A (P-loop) A193-T201 Zinc finger C2H2 type domain C165-H186 C194-H215, C244-H265, C272-H293, C300-H321, C328-H349	g 4165083 growth factor independence-1B Zinc finger protein Rodel, B. et al. Genomics 1998 Dec 15;54(3):580-2	MOTIFS BLAST_GENBANK BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
61	2463542	467	S126 S132 S200 S214 S220 S249 S393 S404 S419 S42 S430 S435 S449 S77 T105 T14 T253 T397 T454 T81 Y313	N114 N335 N354	Zinc finger C2H2 type domain: C6-H28		MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS
62	2486031	550	S115 S272 S317 S429 S441 S444 S62 S81 T302 T360 T364	N238 N249	Homeobox domain: L70-I112	g 1504088 DNA-binding protein	MOTIFS BLAST_GENBANK BLIMPS_BLOCKS
63	2493052	450	S272 S293 S368 S41 S411 S413 T108 T232 T238 T374 T409 T418 T433 T50 Y262 Y396 Y99	N122 N167 N185 N403	Signal peptide: M1-S32 Cytochrome c family heme-binding site: C359-V364 Zinc finger C2H2 type domain: C226-H248, C357-H381	g9230649 zinc finger protein 277 [Homo sapiens] Liang, H. et al. (2000) Genomics 66:226-228	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS
64	2512074	378	S132 S3 T9 T18 S77 S328 T182 S197 T279 S365	N120 N150 N180 N255 N310	Zinc finger C2H2 type domain: C161-H181, C189-H209, C217-H237, C245-H265, C273-H293, C301-H321, C329-H349, C357-H377 Zinc finger protein domain: F10-G48 KRAB box domain: Q5-P79	g 881564 ZNF157	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
65	2646274	233	S14 T34 T127	N53 N67	Protein I transcription initiation factor F84-Y230	g10046714 transcription initiation factor IA protein [Homo sapiens]	MOTIFS BLAST_GENBANK BLAST_PRODOM
66	2672566	102	T66	N11 T99		g 3220232 polyhomeotic Z protein Hemenway, C.S. et al. (1998) Oncogene 16:2541-2547 Haluska, P. et al. (1999) Nucleic Acids Res. 27:2538-2544	MOTIFS
67	2689674	287	T25 T232 S32 S122		Eukaryotic putative RNA-binding region RNP-1 signature: K137-D146, L98-F116 RNA recognition motif: L98-L170, L5-K77	g 1899188 DNA binding protein ACBF AC-rich binding factor	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLAST_PRODOM BLAST_DOMO
68	2703282	208	S11 S23 S117 Y124			g5712754 sex comb on midleg-like-1 protein [Homo sapiens] van de Vosse, E. et al. (1998) Genomics 49:96-102	MOTIFS BLAST_GENBANK
69	2738293	177	S71 T43 S5 T115			g11907923 enhancer of polycomb [Homo sapiens] Shimono, Y. et al. (2000) J. Biol. Chem. 275:39411-39419	MOTIFS BLAST_GENBANK

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
70	2772776	179	T173 S29 S39 T63 T106		Zinc finger protein motif: P104-A166	g6942207 PPARgamma cofactor 2 [Mus musculus] Castillo, G.C. et al. (1999) EMBO J. 18:3676-3687	MOTIFS BLAST_GENBANK BLAST_PRODOM BLAST_DOMO
71	2774476	212	S132 S159 S196 S20 S201 S31 S45 T136 T205 T68		RBP-J Kappa Recombination signal motif: P39-D206	g 2052119 transcription factor RBP-L	MOTIFS BLAST_GENBANK BLAST_PRODOM
72	2804624	256	S103 S202 S238 S244 S33 S7 S85 S89 T112 T212 T245 T99	N6 N101 N132	MAF-1 nuclear matrix protein motif: G82-T210	g3786409 contains similarity to Saccharomyces cerevisiae MAF-1 protein	MOTIFS BLAST_GENBANK BLAST_PRODOM
73	2848225	475	S179 S180 S239 S24 S295 S378 S434 T14 T142 T164 T282 T332 T36 Y136 Y268	N12 N93	Zinc finger C2H2 type domain: F6-R44, C171-Q191, C199-H219, C227-H247, C255-H275, C283-H303, C311-H331, C339-H358, C366-H386, C394-H415, C422-H442, C450-H470 Zinc finger 136: W37-Q145 Zinc finger 137: S259-R335 KRAB box: M1-D76	g 930123 zinc finger protein	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
74	2882241	206	S164 S166 S57 S161 Y29		Helix-loop-helix DNA-binding domain: G58-E110, H27-D165 Myc-type helix-loop-helix motif: E66-K81, C90-E110	g 1184157 Max-interacting transcriptional repressor	MOTIFS BLAST_GENBANK BLAST_PFAM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
75	2939011	596	S152 S203 S212 S244 S272 S477 S481 S516 S536 T121 T164 T200 T204 T229 T339 T361 T363 T396 T537 T543	N84 N510		g 5081374 glucocorticoid modulatory element binding protein-1	MOTIFS BLAST_GENBANK
76	2947188	644	S116 S207 S22 S403 S488 S85 T110 T487 T52 T612	N66 N190 N265 N376	ATP/GTP-binding site motif A (P-loop): G142-S149 Zinc finger C2H2 type domain: C199-H219, C227-H247, C255-H275, C283-H303, C311-H331, C339-H359, C367-H387, C395-H415, C423-H443, C451-H471, C479-H499, C507-H527, C535-H555, C563-H583, C591-H611, C619-H639	g5441615 zinc finger protein	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM
77	3094001	194	T59 T110 S27 S32 S183 Y65	N17	SSU72 start-site selection protein: M1-F194	g4156162 similar to yeast SSU72	MOTIFS BLAST_GENBANK BLAST_PRODOM
78	3110061	536	S21 S134 T157 S214 T76 S83 S252 S404 S462	N132 N380 N389 N445	Zinc finger C2H2 type domain: C202-H222, C230-H250, C258-H277, C286-H306, C314-H334, C342-H362, C370-H390, C398-H418, C426-H446, C454-H474, C482-H502 Transcription factor GATA zinc finger signature: T223-S240 Zinc finger signature: F13-G51, H330-C342	g1017722 repressor transcriptional factor	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
79	3146614	412	S184 T158 T247 S402		Signal peptide: M1-R29 Transcription regulation protein domain: F3-L220 Leucine zipper motif: L80-L101	g2370560 putative translational repressor	MOTIFS BLAST_GENBANK SPSCAN BLAST_PRODOM
80	3295381	482	S161 S216 S318 S352 S385 S408 S456 S72 S99 T177 T18 T84 T88 T9 T94		Zinc finger C2H2 type domain: C178-H198, C206-H226, C234-H254, C262-H282, C290-H310, C346-H366, C374-H394, C402-H422 Zinc finger signature: F10-G48 KRAB box: V8-G69	g6118383 zinc finger protein ZNF223 [Homo sapiens]	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
81	3364774	554	S134 S183 S269 S292 S307 S458 S514 S62 S94 T125 T16 T325 T402 T497	N467	ATP/GTP-binding site motif A (P-loop): A505-S512 Zinc finger C2H2 type domain: C310-H330, C338-H358, C366-H386, C394-H414, C422-H442, C450-H470, C478-H498, C506-H526 KRAB box: V124-S183 Zinc finger signature: F126-P164	g 3818515 zinc finger protein ZNF210	MOTIFS BLAST_GENBANK BLAST_PFAM BLIMPS_BLOCKS BLIMPS_PRINTS BLIMPS_PRODOM BLAST_PRODOM BLAST_DOMO
82	3397777	488	S171 S235 S244 S271 S346 S356 S417 S42 T153 T178 T185	N448	Zinc finger C3HC4 type signature: C30-I40, C15-C59, V9-S64 Interleukin 2 transcription down-regulatory domain: T130-W333 RFP Transforming protein: H67-G347	g11022688 interferon-responsive finger protein 1 middle form [Homo sapiens] Orimo, A. et al. (2000) Genomics 69:143-149	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS PROFILESCAN BLIMPS_PFAM BLAST_PRODOM BLAST_DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
83	3403046	127	T57 S31 S52		Signal peptide: M1-P19 bZIP transcription factors basic domain signature: R40-K55, E33-E97 FOS transforming protein: Q28-K44, N45-D61, L63-L84 DNA-binding transcription factor: A17-L104 Leucine zipper motifs: L63-L84, L70-L91	g 1890635 Jun dimerization protein 1 JDP-1	MOTIFS BLAST_GENBANK HMMER_PFAM BLIMPS_BLOCKS BLAST_PRODOM BLAST_DOMO
84	3538506	532	S143 S170 S185 S191 S282 S283 S327 S340 S457 S49 S497 S72 S99 T147 T156 T223 T30 T331 T449 T501 T71 T86	N280	Signal peptide: M1-A51 C2H2 Zn finger domain: C3-H23, C109-H129, C293-H313, C463-H483, C3-H19	g4056411 Human homolog of Mus musculus wizS protein	MOTIFS BLAST_GENBANK SPSCAN HMMER-PFAM BLIMPS-BLOCKS MOTIFS
85	3575519	353	S110 S194 S210 S240 S256 S266 S285 T189 T198 T278 T326 T60 T77		C3HC4 Zn finger domain: C23-C78, C39-A48, K19-G88 RFP (Zn finger oncogenic protein): K106-K291	g9945010 RING-finger protein MURF [Mus musculus] Spencer, J.A. et al. (2000) J. Cell Biol. 150:771-784	MOTIFS BLAST_GENBANK HMMER-PFAM PROFILESCAN BLAST-DOMO MOTIFS
86	3598694	407	S16 S76 S151 S315 T390			g 5668703 XDRP1	MOTIFS BLAST_GENBANK BLIMPS-BLOCKS
87	3638819	350	S199 S212 S236 Y156 Y184	N12 N210	Transmembrane domain: L310-F330 C2H2 Zn finger domain: G82-A264, Y114-H136, C88-H108, Y142-H164, F170-H192, Y198-H220, F226-H248, P113-S126, L129-G138	g1020145 DNA binding protein	MOTIFS BLAST_GENBANK HMMER HMMER-PFAM BLIMPS-PRINTS BLAST-PRODOM BLAST-DOMO MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
88	3717139	215	S108 S198 S70 T193	N42 N196	Homeobox domain: K33-N96, Q36-E95, E50-A112, R79-N96, T58-L69, L73-R92	g 2632119 Splice variant of homeobox gene Prx3A alternative N-terminal region	MOTIFS BLAST_GENBANK HMMER-PFAM PROFILESCAN BLIMPS-BLOCKS BLIMPS-PRINTS BLAST-PRODOM BLAST-DOMO
89	3892962	489	S227 S43 S113 T230 T97 S196 T392	N110 N200 N308 N319 N366 N450 N480	C2H2 Zn finger domain: C132-H152, L145-G154, C160-H180, C188-H208, C216-H236, C244-H264, C272-H292, C300-H320, P325-S338, C328-H348, C356-H376, C384-H404, C412-H432, C440-H460, C468-H488, G108-H488 Zn finger protein domain: K127-H488	g 488555 zinc finger protein ZNF135	MOTIFS BLAST_GENBANK HMMER-PFAM BLIMPS-BLOCKS BLIMPS-PRINTS BLAST-PRODOM BLAST-DOMO
90	4153521	399	S112 S14 S146 S157 S164 S176 S364 S70 S75 S83 T119 T123 T133 T202 T5 T84	N139 N155 N177 N184	C2H2 Zn finger domain: C315-H335, C231-H251, C343-H363, C287-H307, C203-H223, C259-H279, P340-S353, L216-G225, C371-H391 Zn finger protein domain: V4-W77, F6-G44 KRAB box domain: S2-W73, V4-D72	g7688669 zinc finger protein ZNF140-like protein [Homo sapiens]	MOTIFS BLAST_GENBANK HMMER-PFAM BLIMPS-BLOCKS BLIMPS-PRINTS BLIMPS_PRODOM BLAST-PRODOM BLAST-DOMO
91	4585038	309	S106 S270 S293 S51 S52 S75 S94 T132 T172 T198 T205 T237 T301 T31 T40 T57		transcriptional repressor DNA binding signature: D45-K275	g 4960159 GC-rich sequence DNA-binding factor candidate	MOTIFS BLAST_GENBANK BLAST-PRODOM
92	4674640	361	S28 S30 S352 S56 T170 T176 T206 T77 Y233 Y68	N288	Type I antifreeze protein signature: Q253-F270	g 3779240 zinc finger protein	MOTIFS BLAST_GENBANK BLIMPS-PRINTS

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
93	4676066	540	S115 S135 S151 S202 S301 S34 S39 S405 S490 S497 T368 T508	N222	Signal peptide: M1-S29 RFP (Zn finger oncogenic protein): R381-I526 Adrenomedullin signature: R111-A128	g 3916727 estrogen-responsive B box protein	MOTIFS BLAST_GENBANK SPSCAN BLIMPS_PRINTS BLAST-DOMO
94	4830687	84			Signal peptide: M1-A66 C3HC4 Zn finger domain: C33-E79, C51-C76, N19-K81 Glycoprotein hormone signature: M1-H58	g7649253 hepatocellular carcinoma associated ring finger protein [Homo sapiens]	MOTIFS BLAST_GENBANK HMMER_PFAM SPSCAN PROFILESCAN BLAST-DOMO
95	4880891	1312	S105 S1060 S1063 S1067 S1128 S1129 S1135 S1153 S1159 S1181 S1208 S1222 S1249 S157 S158 S159 S17 S216 S274 S276 S295 S296 S47 S471 S483 S527 S591 S595 S656 S666 S680 S712 S713 S717 S736 S750 S758 S815 S860 S861 S862 S888 S945 S947 T100 T1025 T1034 T1046 T1228 T126 T1293 T140 T31 T41 T481 T507 T508 T531 T793 T801 T811 T812 T876 T939 T971 Y655 Y75 Y89 Y9	N294 N432 N755 N856 N859 N910 N1151 N1226	ARID (AT-Rich Interaction Domain) DNA binding domain: E303-V413 Retinoblastoma binding protein: T742-R1312	g 5257005 Rb binding protein homolog	MOTIFS BLAST_GENBANK HMMER-PFAM BLAST-PRODOM BLAST-DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
96	4909754	504	S109 S181 S304 S357 S36 S384 S389 S417 T194 T212 T246 T255 T323 T333 T365 T490 Y221 Y262 Y85	N309 N355 N421	Transcription factor-like domain: T20-L120 Lymphoid transcription factor ENL: P10-N209 P245 purinoceptor signature: F121-K131	g476099 transcription factor LSF	MOTIFS BLAST_GENBANK BLIMPS_PRINTS BLAST-PRODOM BLAST-DOMO
97	4911931	227	T190 S191 T157 Y62		Transcription factor-like domain: T20-L120 Lymphoid transcription factor ENL: P10-N209 P245 purinoceptor signature: F121-K131	g3878581 Similar to Human AF-9 leukemia protein	MOTIFS BLAST_GENBANK BLAST-PRODOM BLAST-DOMO
98	4920433	233	S43 S50 T62 S77 S110 S131 T165 S17 T69 S194 Y191	N122 N192	Signal peptide: M1-A33 LysR helix-turn helix domain: T97-N122		SPSCAN MOTIFS
99	5042113	511	S176 S203 S276 S278 S430 S436 S455 S56 S99 T12 T173 T239 T247 T274 T372 T449 T504 T509 Y79		Signal peptide: M1-A34 Brain natriuretic peptide: A481-Q499		MOTIFS SPSCAN BLIMPS-PRINTS
100	5083853	247	S102 S110 S123 S19 S190 S58 S84 T150 T163 T212		C-type natriuretic peptide: S44-D54	g 4519621 OASIS (transcription factor) protein	MOTIFS BLAST_GENBANK
101	5283981	276	S160 T68 T126 T168 T193	N20	C2H2 Zn finger domain: K170-H190, F172-H194, C174-H194, L187-D196, E191-H246, Y200-H222, F228-H250, C202-H218, S223-Q252, P227-S240. C230-H250	g 5001720 odd-skipped related 1 protein	MOTIFS BLAST_GENBANK HMMER-PFAM BLIMPS-BLOCKS BLIMPS-PRINTS BLAST-PRODOM BLAST-DOMO

Table 2 (cont.)

Polypeptide SEQ ID NO:		Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
102	5510549	220	S66 T144 S173 T67 S153	N202	C3HC4 Zn finger domain: C168-C208, E164-A219, C168-D211	g9759106 contains similarity to C3HC4-type RING zinc finger protein Sato, S. et al. (1997) DNA Res. 4:215-230	MOTIFS BLAST_GENBANK HMMER-PFAM PROFILESCAN BLAST-DOMO
103	5544862	608	S16 S25 S326 S401 S416 S423 S424 S44 S481 S51 S517 S518 S530 S543 S553 S566 S574 S597 T118 T182 T256 T402 T437 T494 Y552 Y579	N29 N251 N538	Small proline rich protein DNA binding signature: E48-P57, P230-P238 Leucine zipper: L63-L84		MOTIFS BLIMPS-PRINTS
104	5573394	653	G650 S299 S371 S499 S552 S593 S599 S78 T240 T262 T270 T300 T381 T432 T525 T53 T57 T9	N115 N220 N293 N597	Nonstructural polyprotein domain: L118-K284		MOTIFS BLAST_DOMO
105	5850840	154	T9 S19 S25 T30 T63 S138 S149 S21 S92		C3HC4 Zn finger domain: C99-C139, K95-S150	g 3873857 similar to C3HC4 type zinc finger	MOTIFS BLAST_GENBANK HMMER-PFAM PROFILESCAN
106	5942936	337	T8 S10 S12 S67 T77 S138 T214 S84 T162	N25 N65	Helix-loop-helix DNA binding domain: R49-E132, K51-Q104, E57-R72, S84-Q104, E88-L103	g 5059323 hairy and enhancer of split related-1	MOTIFS BLAST_GENBANK HMMER-PFAM BLIMPS-BLOCKS BLAST-DOMO
107	5951431	535	S152 S201 S212 S254 S256 S287 S348 S351 S354 S378 S385 S409 S414 S428 S475 S527 T22 T418 T66 T98 Y210 Y459	N6 N87 N137	Signal peptide: M1-R54 GATA-type Zn finger domain: A19-W74, M1-H95	g9651765 zinc finger protein 289 [Mus musculus]	MOTIFS BLAST_GENBANK HMMER_PFAM SPSCAN BLAST-PRODOM BLAST-DOMO

Table 3

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
108	095210	Reproductive (0.257) Hematopoietic/Immune (0.200) Nervous (0.171)	Cancer (0.429) Inflammation (0.257) Cell Proliferation (0.143)	PBLUESCRIPT
109	157953	Reproductive (0.293) Hematopoietic/Immune (0.207) Gastrointestinal (0.172)	Cancer (0.483) Cell Proliferation (0.310) Inflammation (0.224)	PBLUESCRIPT
110	159196	Reproductive (0.296) Cardiovascular (0.222) Hematopoietic/Immune (0.111) Gastrointestinal (0.111) Urologic (0.111)	Cancer (0.444) Inflammation (0.370) Cell Proliferation (0.222)	PBLUESCRIPT
111	343338	Hematopoietic/Immune (0.300) Nervous (0.260) Reproductive (0.140)	Cancer (0.380) Inflammation (0.320) Cell Proliferation (0.220)	PBLUESCRIPT
112	402386	Hematopoietic/Immune (0.381) Reproductive (0.190) Gastrointestinal (0.143) Nervous (0.143)	Inflammation (0.476) Cancer (0.333)	PBLUESCRIPT
113	456487	Reproductive (0.248) Nervous (0.198) Gastrointestinal (0.132)	Cancer (0.488) Inflammation (0.207) Cell Proliferation (0.165)	PBLUESCRIPT
114	490256	Developmental (0.231) Reproductive (0.231) Endocrine (0.154) Hematopoietic/Immune (0.154) Gastrointestinal (0.154)	Cancer (0.231) Cell Proliferation (0.231) Inflammation (0.231)	PBLUESCRIPT
115	494740	Gastrointestinal (0.209) Nervous (0.209) Hematopoietic/Immune (0.186)	Inflammation (0.395) Cancer (0.302) Cell Proliferation (0.209)	PBLUESCRIPT
116	507475	Reproductive (0.246) Hematopoietic/Immune (0.180) Gastrointestinal (0.148)	Cancer (0.426) Cell Proliferation (0.230) Inflammation (0.230)	PBLUESCRIPT
117	531581	Hematopoietic/Immune (0.231) Reproductive (0.231) Nervous (0.154)	Cancer (0.385) Cell Proliferation (0.231) Inflammation (0.205)	PSPORT1

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
118	675190	Reproductive (0.389) Nervous (0.278) Cardiovascular (0.111) Urologic (0.111)	Cancer (0.722) Inflammation (0.111) Trauma (0.111)	PSPORT1
119	685434	Reproductive (0.333) Nervous (0.194) Cardiovascular (0.111) Hematopoietic/Immune (0.111)	Cancer (0.556) Inflammation (0.278) Cell Proliferation (0.111)	PSPORT1
120	788663	Reproductive (0.303) Cardiovascular (0.182) Hematopoietic/Immune (0.152)	Cancer (0.455) Inflammation (0.303) Cell Proliferation (0.212)	PSPORT1
121	870100	Reproductive (0.298) Nervous (0.170) Cardiovascular (0.128)	Cancer (0.660) Inflammation (0.170) Cell Proliferation (0.149)	PSPORT1
122	879500	Reproductive (0.203) Gastrointestinal (0.153) Hematopoietic/Immune (0.136)	Cancer (0.373) Inflammation (0.322) Cell Proliferation (0.203)	PSPORT1
123	975377	Reproductive (0.215) Nervous (0.177) Hematopoietic/Immune (0.152)	Cancer (0.418) Inflammation (0.291) Cell Proliferation (0.127)	PSPORT1
124	1208721	Reproductive (0.282) Nervous (0.200) Hematopoietic/Immune (0.141)	Cancer (0.471) Inflammation (0.282) Cell Proliferation (0.141)	PSPORT1
125	1234329	Reproductive (0.277) Nervous (0.191) Cardiovascular (0.128) Hematopoietic/Immune (0.128)	Cancer (0.553) Cell Proliferation (0.234) Inflammation (0.213)	pINCY
126	1238747	Hematopoietic/Immune (0.283) Gastrointestinal (0.167) Reproductive (0.150)	Cancer (0.400) Inflammation (0.300) Trauma (0.117) Cell Proliferation (0.117)	PSPORT1
127	1265980	Nervous (0.900) Developmental (0.100)	Cell Proliferation (0.400) Inflammation (0.200) Neurological (0.200)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
128	1297333	Developmental (0.273) Reproductive (0.273) Hematopoietic/Immune (0.273)	Cell Proliferation (0.273) Inflammation (0.273) Cancer (0.182)	pINCY
129	1312824	Reproductive (0.238) Hematopoietic/Immune (0.222) Gastrointestinal (0.159)	Cancer (0.429) Inflammation (0.238) Cell Proliferation (0.175)	pINCY
130	1359294	Reproductive (0.219) Nervous (0.157) Gastrointestinal (0.145)	Cancer (0.438) Inflammation (0.247) Cell Proliferation (0.188)	pINCY
131	1377380	Reproductive (0.385) Developmental (0.231) Hematopoietic/Immune (0.231)	Cancer (0.538) Cell Proliferation (0.385) Inflammation (0.154)	pINCY
132	1383473	Reproductive (0.318) Nervous (0.182) Hematopoietic/Immune (0.121)	Cancer (0.515) Inflammation (0.288) Cell Proliferation (0.197)	pINCY
133	1388860	Cardiovascular (0.167) Nervous (0.167) Reproductive (0.167)	Cancer (0.444) Inflammation (0.222) Cell Proliferation (0.167) Trauma (0.167)	pINCY
134	1395322	Nervous (0.261) Reproductive (0.261)	Cancer (0.478) Inflammation (0.304) Cell Proliferation (0.130) Trauma (0.130)	pINCY
135	1419370	Reproductive (0.290) Nervous (0.246) Gastrointestinal (0.116)	Cancer (0.522) Cell Proliferation (0.188) Inflammation (0.130)	pINCY
136	1429773	Reproductive (0.255) Gastrointestinal (0.160) Cardiovascular (0.128)	Cancer (0.521) Inflammation (0.191) Cell Proliferation (0.170)	pINCY
137	1470820	Reproductive (0.231) Developmental (0.154) Gastrointestinal (0.154) Hematopoietic/Immune (0.154) Nervous (0.154) Gastrointestinal (0.154)	Cancer (0.385) Cell Proliferation (0.231) Inflammation (0.231)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
138	1483455	Nervous (0.222) Urologic (0.156) Cardiovascular (0.111) Developmental (0.111) Reproductive (0.111)	Cancer (0.422) Cell Proliferation (0.244) Inflammation (0.244)	pINCY
139	1527064	Reproductive (0.262) Nervous (0.169) Cardiovascular (0.131)	Cancer (0.481) Cell Proliferation (0.257) Inflammation (0.224)	PBLUESCRIPT
140	1557491	Nervous (0.222) Reproductive (0.222) Cardiovascular (0.167)	Cancer (0.444) Neurological (0.167) Cell Proliferation (0.111) Inflammation (0.111)	pINCY
141	1576862	Gastrointestinal (0.280) Hematopoietic/Immune (0.240) Nervous (0.160)	Cancer (0.480) Inflammation (0.320) Cell Proliferation (0.120)	pINCY
142	1609731	Gastrointestinal (0.286) Nervous (0.286) Cardiovascular (0.143) Developmental (0.143) Urologic (0.143)	Cancer (0.429) Cell Proliferation (0.286) Neurological (0.143) Trauma (0.143)	pINCY
143	1674538	Nervous (0.364) Cardiovascular (0.364) Gastrointestinal (0.182)	Cancer (0.364) Cell Proliferation (0.182)	pINCY
144	1675287	Reproductive (0.373) Hematopoietic/Immune (0.169) Urologic (0.119)	Cancer (0.492) Inflammation (0.305) Cell Proliferation (0.153)	pINCY
145	1693903	Reproductive (0.212) Hematopoietic/Immune (0.186) Nervous (0.177)	Cancer (0.434) Inflammation (0.327) Cell Proliferation (0.257)	pINCY
146	1702962	Reproductive (0.389) Cardiovascular (0.167) Gastrointestinal (0.167)	Cancer (0.556) Trauma (0.222)	pINCY
147	1712916	Reproductive (1.000)	Cancer (1.000)	pINCY
148	1748313	Nervous (0.265) Reproductive (0.162) Hematopoietic/Immune (0.147)	Cancer (0.456) Inflammation (0.279) Cell Proliferation (0.176)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
149	1754833	Hematopoietic/Immune (0.208) Gastrointestinal (0.189) Nervous (0.151)	Inflammation (0.377) Cancer (0.358) Cell Proliferation (0.170)	pINCY
150	1798701	Nervous (0.237) Reproductive (0.212) Gastrointestinal (0.119)	Cancer (0.449) Inflammation (0.237) Cell Proliferation (0.178)	pINCY
151	1842496	Reproductive (0.254) Nervous (0.187) Gastrointestinal (0.119)	Cancer (0.500) Cell Proliferation (0.224) Inflammation (0.149)	PSPORT1
152	1868613	Hematopoietic/Immune (0.286) Reproductive (0.257) Cardiovascular (0.114) Gastrointestinal (0.114)	Cell Proliferation (0.486) Cancer (0.400) Inflammation (0.286)	pINCY
153	1870609	Nervous (0.207) Reproductive (0.195) Gastrointestinal (0.159)	Cancer (0.439) Inflammation (0.244) Cell Proliferation (0.171)	pINCY
154	1871961	Reproductive (0.268) Nervous (0.196) Hematopoietic/Immune (0.113)	Cancer (0.474) Cell Proliferation (0.247) Inflammation (0.165)	pINCY
155	1876258	Hematopoietic/Immune (0.600) Cardiovascular (0.200) Reproductive (0.100) Gastrointestinal (0.100)	Inflammation (0.400) Trauma (0.200) Cancer (0.100)	pINCY
156	1929822	Reproductive (0.255) Nervous (0.160) Hematopoietic/Immune (0.128) Gastrointestinal (0.128)	Cancer (0.479) Inflammation (0.223) Cell Proliferation (0.213)	pINCY
157	1970095	Nervous (0.205) Reproductive (0.205) Cardiovascular (0.133)	Cancer (0.385) Inflammation (0.256) Cell Proliferation (0.159)	PBLUESCRIPT
158	1975473	Gastrointestinal (0.464) Reproductive (0.250)	Cancer (0.536) Inflammation (0.214) Cell Proliferation (0.179)	pINCY
159	1976527	Reproductive (0.247) Gastrointestinal (0.192) Nervous (0.178)	Cancer (0.466) Inflammation (0.247) Cell Proliferation (0.233)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
160	2108023	Reproductive (0.750) Nervous (0.250)	Cancer (0.500) Inflammation (0.250) Trauma (0.250)	PSPORT1
161	2135746	Nervous (0.321) Cardiovascular (0.214) Reproductive (0.143)	Cancer (0.500) Inflammation (0.214) Trauma (0.179)	pINCY
162	2154810	Cardiovascular (0.222) Developmental (0.222) Hematopoietic/Immune (0.222)	Cancer (0.333) Cell Proliferation (0.333) Inflammation (0.222)	pINCY
163	2228991	Hematopoietic/Immune (0.500) Gastrointestinal (0.167) Reproductive (0.167)	Inflammation (0.333) Cancer (0.250) Cell Proliferation (0.167)	pINCY
164	2241206	Cardiovascular (0.269) Gastrointestinal (0.154) Nervous (0.154)	Cancer (0.346) Cell Proliferation (0.346) Inflammation (0.308)	pINCY
165	2259590	Reproductive (0.375) Urologic (0.250) Hematopoietic/Immune (0.125) Developmental (0.125) Endocrine (0.125)	Cancer (0.500) Cell Proliferation (0.250) Inflammation (0.250)	PSPORT1
166	2307537	Reproductive (0.241) Gastrointestinal (0.138) Nervous (0.138)	Cancer (0.414) Cell Proliferation (0.241) Inflammation (0.241)	PSPORT1
167	2440675	Hematopoietic/Immune (0.600) Cardiovascular (0.200) Reproductive (0.100) Gastrointestinal (0.100)	Inflammation (0.400) Trauma (0.200) Cell Proliferation (0.100) Cancer (0.100)	pINCY
168	2463542	Reproductive (0.333) Nervous (0.250) Hematopoietic/Immune (0.125)	Cancer (0.542) Inflammation (0.292) Trauma (0.125)	pINCY
169	2486031	Reproductive (0.333) Cardiovascular (0.167) Gastrointestinal (0.167) Nervous (0.167)	Cancer (0.333) Cell Proliferation (0.250)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
170	2493052	Nervous (0.200) Gastrointestinal (0.171) Reproductive (0.171)	Cancer (0.429) Cell Proliferation (0.343) Inflammation (0.229)	pINCY
171	2512074	Hematopoietic/Immune (0.333) Reproductive (0.333) Nervous (0.250)	Inflammation (0.500) Cancer (0.417) Cell Proliferation (0.333)	pINCY
172	2646274	Gastrointestinal (0.207) Reproductive (0.207) Developmental (0.138)	Cancer (0.379) Inflammation (0.310) Cell Proliferation (0.207)	pINCY
173	2672566	Nervous (0.400) Gastrointestinal (0.200) Cardiovascular (0.100) Hematopoietic/Immune (0.100) Reproductive (0.100)	Cancer (0.600) Cell Proliferation (0.100) Inflammation (0.100) Neurological (0.100)	pINCY
174	2689674	Gastrointestinal (0.191) Reproductive (0.191) Hematopoietic/Immune (0.170)	Cancer (0.489) Inflammation (0.191) Cell Proliferation (0.149)	pINCY
175	2703282	Reproductive (0.409) Nervous (0.136) Gastrointestinal (0.114) Hematopoietic/Immune (0.114)	Cancer (0.409) Inflammation (0.386) Cell Proliferation (0.205)	pINCY
176	2738293	Reproductive (0.333) Cardiovascular (0.167) Gastrointestinal (0.167)	Cancer (0.416) Cell Proliferation (0.167) Inflammation (0.167) Trauma (0.167)	pINCY
177	2772776	Reproductive (0.232) Gastrointestinal (0.152) Nervous (0.134)	Cancer (0.500) Inflammation (0.205) Cell Proliferation (0.152)	pINCY
178	2774476	Gastrointestinal (0.712) Developmental (0.143) Nervous (0.143)	Trauma (0.429) Cancer (0.286) Cell Proliferation (0.286)	pINCY
179	2804624	Reproductive (0.252) Gastrointestinal (0.173) Cardiovascular (0.150)	Cancer (0.480) Inflammation (0.236) Trauma (0.134)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
180	2848225	Reproductive (0.385) Hematopoietic/Immune (0.231) Gastrointestinal (0.154)	Cancer (0.385) Trauma (0.308) Cell Proliferation (0.154) Inflammation (0.154)	pINCY
181	2882241	Hematopoietic/Immune (0.259) Gastrointestinal (0.185) Reproductive (0.185)	Cancer (0.519) Inflammation (0.333) Cell Proliferation (0.148)	pINCY
182	2939011	Hematopoietic/Immune (0.263) Cardiovascular (0.158) Gastrointestinal (0.158) Urologic (0.158) Nervous (0.158)	Cancer (0.316) Cell Proliferation (0.316) Inflammation (0.316)	pINCY
183	2947188	Nervous (0.308) Gastrointestinal (0.154) Reproductive (0.154)	Cancer (0.346) Inflammation (0.308) Cell Proliferation (0.154) Trauma (0.154)	pINCY
184	3094001	Reproductive (0.266) Gastrointestinal (0.160) Nervous (0.160)	Cancer (0.500) Inflammation (0.223) Cell Proliferation (0.160)	pINCY
185	3110061	Cardiovascular (0.333) Hematopoietic/Immune (0.267) Nervous (0.200) Reproductive (0.200)	Inflammation (0.467) Cancer (0.400) Cell Proliferation (0.267)	pINCY
186	3146614	Reproductive (0.326) Nervous (0.209) Gastrointestinal (0.163)	Cancer (0.512) Inflammation (0.186)	pINCY
187	3295381	Hematopoietic/Immune (0.267) Musculoskeletal (0.200) Reproductive (0.200)	Cancer (0.533) Inflammation (0.400)	pINCY
188	3364774	Nervous (0.375) Gastrointestinal (0.208) Reproductive (0.167)	Cancer (0.583) Cell Proliferation (0.250)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
189	3397777	Reproductive (0.231) Cardiovascular (0.154) Gastrointestinal (0.154) Endocrine (0.154) Hematopoietic/Immune (0.154)	Cancer (0.462) Inflammation (0.385)	pINCY
190	3403046	Reproductive (0.500) Hematopoietic/Immune (0.250) Nervous (0.250)	Cancer (0.500) Inflammation (0.250)	pINCY
191	3538506	Reproductive (0.438) Gastrointestinal (0.188) Hematopoietic/Immune (0.188) Nervous (0.188)	Cancer (0.625) Trauma (0.250) Cell Proliferation (0.188)	pINCY
192	3575519	Cardiovascular (0.455) Musculoskeletal (0.273)	Trauma (0.455) Cancer (0.273)	pINCY
193	3598694	Nervous (0.247) Reproductive (0.247)	Cancer (0.575) Cell Proliferation (0.233) Inflammation (0.110)	pINCY
194	3638819	Reproductive (0.333) Nervous (0.222) Gastrointestinal (0.111)	Cancer (0.556) Inflammation (0.185)	pINCY
195	3717139	Hematopoietic/Immune (0.500) Reproductive (0.500)	Cancer (0.500) Inflammation (0.500)	pINCY
196	3892962	Reproductive (0.455) Musculoskeletal (0.182) Nervous (0.182)	Cancer (0.909) Cell Proliferation (0.182)	pINCY
197	4153521	Nervous (0.281) Urologic (0.156) Reproductive (0.141)	Cancer (0.453) Inflammation (0.203) Cell Proliferation (0.156)	pINCY
198	4585038	Cardiovascular (0.261) Nervous (0.261) Hematopoietic/Immune (0.174)	Cancer (0.261) Inflammation (0.261) Cell Proliferation (0.130) Trauma (0.130)	pINCY
199	4674640	Nervous (0.283) Reproductive (0.239) Gastrointestinal (0.174)	Cancer (0.391) Inflammation (0.304) Cell Proliferation (0.109) Neurological (0.109)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
200	4676066	Reproductive (0.317) Cardiovascular (0.175) Gastrointestinal (0.175) Nervous (0.175)	Cancer (0.508) Inflammation (0.159) Trauma (0.127)	pINCY
201	4830687	Reproductive (0.276) Gastrointestinal (0.147) Nervous (0.147)	Cancer (0.482) Cell Proliferation (0.218) Inflammation (0.194)	pINCY
202	4880891	Hematopoietic/Immune (0.190) Gastrointestinal (0.159) Nervous (0.159)	Cancer (0.381) Inflammation (0.333) Cell Proliferation (0.222)	pINCY
203	4909754	Reproductive (0.333) Hematopoietic/Immune (0.190) Gastrointestinal (0.143)	Cancer (0.381) Inflammation (0.333) Cell Proliferation (0.286)	pINCY
204	4911931	Nervous (0.219) Hematopoietic/Immune (0.188) Reproductive (0.125) Cardiovascular (0.125)	Cancer (0.375) Cell Proliferation (0.312) Inflammation (0.219)	pINCY
205	4920433	Reproductive (1.000)	Inflammation (1.000)	pINCY
206	5042113	Gastrointestinal (0.206) Reproductive (0.159) Nervous (0.159)	Cancer (0.413) Inflammation (0.206) Cell Proliferation (0.190)	pINCY
207	5083853	Gastrointestinal (0.250) Hematopoietic/Immune (0.250) Musculoskeletal (0.125) Reproductive (0.125) Cardiovascular (0.125) Nervous (0.125)	Cancer (0.375) Inflammation (0.375) Neurological (0.125)	pINCY
208	5283981	Reproductive (0.686)	Cancer (0.514) Inflammation (0.171) Cell Proliferation (0.114)	pINCY
209	5510549	Hematopoietic/Immune (0.222) Reproductive (0.222) Nervous (0.148)	Cancer (0.593) Inflammation (0.148) Trauma (0.111) Cell Proliferation (0.111)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:		Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
210	5544862	Endocrine (0.222) Nervous (0.222) Reproductive (0.222) Gastrointestinal (0.111) Hematopoietic/Immune (0.111)	Trauma (0.333) Inflammation (0.222) Cell Proliferation (0.111) Neurological (0.111) Cancer (0.111)	pINCY
211	5573394	Reproductive (0.194) Cardiovascular (0.149) Hematopoietic/Immune (0.149)	Cancer (0.463) Inflammation (0.343) Cell Proliferation (0.164)	pINCY
212	5850840	Nervous (0.295) Reproductive (0.268) Cardiovascular (0.128)	Cancer (0.416) Inflammation (0.208) Cell Proliferation (0.134)	pINCY
213	5942936	Nervous (0.444) Reproductive (0.333) Cardiovascular (0.111) Musculoskeletal (0.111)	Cancer (0.556) Inflammation (0.333) Neurological (0.111) Trauma (0.111)	pINCY
214	5951431	Reproductive (0.317) Nervous (0.194) Gastrointestinal (0.151)	Cancer (0.518) Inflammation (0.194) Cell Proliferation (0.180)	pINCY

Table 4

Nucleotide SEQ ID NO:		Library	Library Description
108	095210	PITUNOT01	Library was constructed using RNA isolated from pituitary glands removed from a pool of 18 male and female Caucasian donors, 16 to 70 years old, who died from trauma. (RNA came from Clontech.)
109	157953	THP1PLB02	Library was constructed by reamplification of a library made using RNA isolated from THP-1 cells cultured for 48 hours with 100 ng/ml phorbol ester (PMA), followed by a 4-hour culture in media containing 1 ug/ml LPS. THP-1 is a human promonocyte line derived from the peripheral blood of a 1-year-old male with acute monocytic leukemia. One million primary clones were amplified following phage packaging.
110	159196	ADENINB01	Library was constructed using RNA isolated from the inflamed adenoid tissue of a 3-year-old child. (RNA came from Clontech.)
111	343338	THYMNOT02	Library was constructed using RNA isolated from thymus tissue removed from a 3-year-old Caucasian male, who died from drowning.
112	402386	TMLR3DT01	Library was constructed using RNA isolated from non-adherent and adherent peripheral blood mononuclear cells collected from two unrelated Caucasian male donors (25 and 29 years old).
113	456487	KERANOT01	Library was constructed using RNA isolated from neonatal keratinocytes obtained from the leg skin of a spontaneously aborted black male.
114	490256	HNT2AGT01	Library was constructed at Stratagene (STR937233), using RNA isolated from the hNT2 cell line derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor. Cells were treated with retinoic acid for 5 weeks, with mitotic inhibitors for two weeks and allowed to mature for an additional 4 weeks in conditioned medium.
115	494740	HNT2NOT01	Library was constructed at Stratagene (STR937230), using RNA isolated from the hNT2 cell line (derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor).
116	507475	TMLR3DT01	Library was constructed using RNA isolated from non-adherent and adherent peripheral blood mononuclear cells collected from two unrelated Caucasian male donors (25 and 29 years old).
117	531581	BRAINOT03	Library was constructed using RNA isolated from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.
118	675190	CRBLNOT01	Library was constructed using RNA isolated from the cerebellum tissue of a 69-year-old Caucasian male who died from chronic obstructive pulmonary disease. Patient history included myocardial infarction, hypertension, and osteoarthritis.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
119	685434	UTRSNOT02	Library was constructed using RNA isolated from uterine tissue removed from a 34-year-old Caucasian female during a vaginal hysterectomy. Patient history included mitral valve disorder. Family history included stomach cancer, congenital heart anomaly, irritable bowel syndrome, ulcerative colitis, colon cancer, cerebrovascular disease, type II diabetes, and depression.
120	788663	PROSNOT05	Library was constructed using RNA isolated from diseased prostate tissue removed from a 67-year-old Caucasian male during radical prostatectomy and lymph node biopsy. This library has been determined to contain some tumor cells. Pathology indicated adenofibromatous hyperplasia was present. Pathology for the associated tumor tissue indicated adenocarcinoma Gleason grade 3+3. Patient history included coronary artery disease, stomach ulcer, and osteoarthritis. Family history included congestive heart failure.
121	870100	LUNGAST01	Library was constructed using RNA isolated from the lung tissue of a 17-year-old Caucasian male, who died from head trauma. Patient history included asthma.
122	879500	THYRNOT02	Library was constructed using RNA isolated from the diseased thyroid tissue of a 16-year-old Caucasian female with Graves' disease (hyperthyroidism).
123	975377	MUSCNOT02	Library was constructed using RNA isolated from the psoas muscle tissue of a 12-year-old Caucasian male.
124	1208721	BRSTNOT02	Library was constructed using RNA isolated from diseased breast tissue removed from a 55-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated proliferative fibrocysytic changes characterized by apocrine metaplasia, sclerosing adenosis, cyst formation, and ductal hyperplasia without atypia. Pathology for the associated tumor tissue indicated an invasive grade 4 mammary adenocarcinoma. Patient history included atrial tachycardia and a benign neoplasm. Family history included cardiovascular and cerebrovascular disease.
125	1234329	LUNGFET03	Library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.
126	1238747	LUNGTUT02	Library was constructed using RNA isolated from the metastatic lung tumor tissue of a 79-year-old Caucasian male. Pathology indicated a grade 4 carcinoma of the upper and lower left lobes. Patient history included a benign prostate neoplasm, atherosclerosis, and tobacco use.
127	1265980	BRAINOT09	Library was constructed using RNA isolated from brain tissue removed from a Caucasian male fetus, who died at 23 weeks' gestation.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
128	1297333	BRSTNOT07	Library was constructed using RNA isolated from diseased breast tissue removed from a 43-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated mildly proliferative fibrocystic changes with epithelial hyperplasia, papillomatosis, and duct ectasia. Pathology for the associated tumor tissue indicated invasive grade 4, nuclear grade 3 mammary adenocarcinoma with extensive comedo necrosis. Family history included epilepsy, cardiovascular disease, and type II diabetes.
129	1312824	BLADTUT02	Library was constructed using RNA isolated from bladder tumor tissue removed from an 80-year-old Caucasian female during a radical cystectomy and lymph node excision. Pathology indicated grade 3 invasive transitional cell carcinoma. Family history included acute renal failure, osteoarthritis, and atherosclerosis.
130	1359294	LUNGNOT12	Library was constructed using RNA isolated from lung tissue removed from a 78-year-old Caucasian male during a segmental lung resection and regional lymph node resection. Pathology indicated fibrosis pleura was puckered, but not invaded. Pathology for the associated tumor tissue indicated an invasive pulmonary grade 3 adenocarcinoma. Patient history included cerebrovascular disease, arteriosclerotic coronary artery disease, thrombophlebitis, chronic obstructive pulmonary disease, and asthma. Family history included intracranial hematoma, cerebrovascular disease, arteriosclerotic coronary artery disease, and type I diabetes.
131	1377380	LUNGNOT10	Library was constructed using RNA isolated from the lung tissue of a Caucasian male fetus, who died at 23 weeks' gestation.
132	1383473	BRAITUT08	Library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe of a 47-year-old Caucasian male during excision of cerebral meningeal tissue. Pathology indicated grade 4 fibrillary astrocytoma with focal tumoral radionecrosis. Patient history included cerebrovascular disease, deficiency anemia, hyperlipidemia, epilepsy, and tobacco use. Family history included cerebrovascular disease and a malignant prostate neoplasm.
133	1388860	EOSINOT01	Library was constructed using RNA isolated from microscopically normal eosinophils from 31 non-allergic donors.
134	1395322	THYRNOT03	Library was constructed using RNA isolated from thyroid tissue removed from the left thyroid of a 28-year-old Caucasian female during a complete thyroidectomy. Pathology indicated a small nodule of adenomatous hyperplasia present in the left thyroid. Pathology for the associated tumor tissue indicated dominant follicular adenoma, forming a well-encapsulated mass in the left thyroid.
135	1419370	KIDNNOT09	Library was constructed using RNA isolated from the kidney tissue of a Caucasian male fetus, who died at 23 weeks' gestation.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
136	1429773	SINTBST01	Library was constructed using RNA isolated from ileum tissue obtained from an 18-year-old Caucasian female during bowel anastomosis. Pathology indicated Crohn's disease of the ileum, involving 15 cm of the small bowel. Family history included cerebrovascular disease and atherosclerotic coronary artery disease.
137	1470820	PANCTUT02	Library was constructed using RNA isolated from pancreatic tumor tissue removed from a 45-year-old Caucasian female during radical pancreaticoduodenectomy. Pathology indicated a grade 4 anaplastic carcinoma. Family history included benign hypertension, hyperlipidemia and atherosclerotic coronary artery disease.
138	1483455	CORPNOT02	Library was constructed using RNA isolated from diseased corpus callosum tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.
139	1527064	UCMCL5T01	Library was constructed using RNA isolated from mononuclear cells obtained from the umbilical cord blood of 12 individuals. The cells were cultured for 12 days with IL-5 before RNA was obtained from the pooled lysates.
140	1557491	BLADTUT04	Library was constructed using RNA isolated from bladder tumor tissue removed from a 60-year-old Caucasian male during a radical cystectomy, prostatectomy, and vasectomy. Pathology indicated grade 3 transitional cell carcinoma in the left bladder wall. Carcinoma in-situ was identified in the dome and trigone. Patient history included tobacco use. Family history included type I diabetes, malignant neoplasm of the stomach, atherosclerotic coronary artery disease, and acute myocardial infarction.
141	1576862	LNODNOT03	Library was constructed using RNA isolated from lymph node tissue obtained from a 67-year-old Caucasian male during a segmental lung resection and bronchoscopy. This tissue was extensively necrotic with 10% viable tumor. Pathology for the associated tumor tissue indicated invasive grade 3-4 squamous cell carcinoma. Patient history included hemangioma. Family history included atherosclerotic coronary artery disease, benign hypertension, and congestive heart failure.
142	1609731	COLNTUT06	Library was constructed using RNA isolated from colon tumor tissue obtained from a 45-year-old Caucasian female during a total colectomy and total abdominal hysterectomy. Pathology indicated invasive grade 2 colonic adenocarcinoma forming a cecal mass. Patient history included benign neoplasms of the rectum and anus, multiple sclerosis and mitral valve disorder. Previous surgeries included a polypectomy. Family history included type I diabetes, cerebrovascular disease, malignant skin neoplasm, hypertension, atherosclerotic coronary artery disease and malignant neoplasm of the colon.

Table 4 (cont.)

Nucleotide SEQ	ID NO:	Library	Library Description
143	1674538	BLADNOT05	Library was constructed using RNA isolated from bladder tissue removed from a 60-year-old Caucasian male during a radical cystectomy, prostatectomy, and vasectomy. Pathology for the associated tumor tissue indicated grade 3 transitional cell carcinoma. Carcinoma in-situ was identified in the dome and trigone. Patient history included tobacco use.
144	1675287	BLADNOT05	Library was constructed using RNA isolated from bladder tissue removed from a 60-year-old Caucasian male during a radical cystectomy, prostatectomy, and vasectomy. Pathology for the associated tumor tissue indicated grade 3 transitional cell carcinoma. Carcinoma in-situ was identified in the dome and trigone. Patient history included tobacco use.
145	1693903	COLNNOT23	Library was constructed using RNA isolated from diseased colon tissue removed from a 16-year-old Caucasian male during a total colectomy with abdominal/perineal resection. Pathology indicated gastritis and pancolonitis consistent with the acute phase of ulcerative colitis. Inflammation was more severe in the transverse colon, with inflammation confined to the mucosa. There was only mild involvement of the ascending and sigmoid colon. Family history included irritable bowel syndrome.
146	1702962	DUODNOT02	Library was constructed using RNA isolated from duodenal tissue of an 8-year-old Caucasian female, who died from head trauma. Serology was positive for cytomegalovirus (CMV).
147	1712916	PROSNOT16	Library was constructed using RNA isolated from diseased prostate tissue removed from a 68-year-old Caucasian male during a radical prostatectomy. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 3+4). The patient presented with elevated prostate specific antigen (PSA). During this hospitalization, the patient was diagnosed with myasthenia gravis. Patient history included osteoarthritis, and type II diabetes. Family history included benign hypertension, acute myocardial infarction, hyperlipidemia, and arteriosclerotic coronary artery disease.
148	1748313	STOMTUT02	Library was constructed using RNA isolated from stomach tumor tissue obtained from a 68-year-old Caucasian female during a partial gastrectomy. Pathology indicated a malignant lymphoma of diffuse large-cell type. Previous surgeries included cholecystectomy. Patient history included thalassemia. Family history included acute leukemia, malignant esophagus and stomach neoplasms, and atherosclerotic coronary artery disease.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
149	1754833	LIVRTUT01	Library was constructed using RNA isolated from liver tumor tissue removed from a 51-year-old Caucasian female during a hepatic lobectomy. Pathology indicated metastatic grade 3 adenocarcinoma consistent with colon cancer. Family history included a malignant neoplasm of the liver.
150	1798701	COLNNOT27	Library was constructed using RNA isolated from diseased cecal tissue removed from a 31-year-old Caucasian male during a total intra-abdominal colectomy, appendectomy, and permanent ileostomy. Pathology indicated severe active Crohn's disease involving the colon from the cecum to the rectum. There were deep rake-like ulcerations that spared the intervening mucosa. The ulcers extended into the muscularis, and there was transmural inflammation. Patient history included an irritable colon. Previous surgeries included a colonscopy.
151	1842496	COLNNOT07	Library was constructed using RNA isolated from colon tissue removed from a 60-year-old Caucasian male during a left hemicolectomy.
152	1868613	SKINBIT01	Library was constructed using RNA isolated from diseased skin tissue of the left lower leg. Patient history included erythema nodosum of the left lower leg.
153	1870609	SKINBIT01	Library was constructed using RNA isolated from diseased skin tissue of the left lower leg. Patient history included erythema nodosum of the left lower leg.
154	1871961	LEUKNOT02	Library was constructed using RNA isolated from white blood cells of a 45-year-old female with blood type O+. The donor tested positive for cytomegalovirus (CMV).
155	1876258	LEUKNOT02	Library was constructed using RNA isolated from white blood cells of a 45-year-old female with blood type O+. The donor tested positive for cytomegalovirus (CMV).
156	1929822	COLNTUT03	Library was constructed using RNA isolated from colon tumor tissue obtained from the sigmoid colon of a 62-year-old Caucasian male during a sigmoidectomy and permanent colostomy. Pathology indicated invasive grade 2 adenocarcinoma. One lymph node contained metastasis with extranodal extension. Patient history included hyperlipidemia, cataract disorder, and dermatitis. Family history included benign hypertension, atherosclerotic coronary artery disease, hyperlipidemia, breast cancer and prostate cancer.
157	1970095	UCMCL5T01	Library was constructed using RNA isolated from mononuclear cells obtained from the umbilical cord blood of 12 individuals. The cells were cultured for 12 days with IL-5 before RNA was obtained from the pooled lysates.
158	1975473	PANCTUT02	Library was constructed using RNA isolated from pancreatic tumor tissue removed from a 45-year-old Caucasian female during radical pancreaticoduodenectomy. Pathology indicated a grade 4 anaplastic carcinoma. Family history included benign hypertension, hyperlipidemia and atherosclerotic coronary artery disease.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
159	1976527	PANCTUT02	Library was constructed using RNA isolated from pancreatic tumor tissue removed from a 45-year-old Caucasian female during radical pancreaticoduodenectomy. Pathology indicated a grade 4 anaplastic carcinoma. Family history included benign hypertension, hyperlipidemia and atherosclerotic coronary artery disease.
160	2108023	BRAITUT03	Library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe a 17-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated a grade 4 fibrillary giant and small-cell astrocytoma. Family history included benign hypertension and cerebrovascular disease.
161	2135746	ENDCNOT01	Library was constructed using RNA isolated from endothelial cells removed from the coronary artery of a 58-year-old Hispanic male.
162	2154810	BRAINOT09	Library was constructed using RNA isolated from brain tissue removed from a Caucasian male fetus, who died at 23 weeks' gestation.
163	2228991	PROSNOT16	Library was constructed using RNA isolated from diseased prostate tissue removed from a 68-year-old Caucasian male during a radical prostatectomy. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 3+4). The patient presented with elevated prostate specific antigen (PSA). During this hospitalization, the patient was diagnosed with myasthenia gravis. Patient history included osteoarthritis, and type II diabetes. Family history included benign hypertension, acute myocardial infarction, hyperlipidemia, and arteriosclerotic coronary artery disease.
164	2241206	PANCTUT02	Library was constructed using RNA isolated from pancreatic tumor tissue removed from a 45-year-old Caucasian female during radical pancreaticoduodenectomy. Pathology indicated a grade 4 anaplastic carcinoma. Family history included benign hypertension, hyperlipidemia and atherosclerotic coronary artery disease.
165	2259590	OVARTUT01	Library was constructed using RNA isolated from ovarian tumor tissue removed from a 43-year-old Caucasian female during removal of the fallopian tubes and ovaries. Pathology indicated grade 2 mucinous cystadenocarcinoma involving the entire left ovary. Patient history included mitral valve disorder, pneumonia, and viral hepatitis. Family history included atherosclerotic coronary artery disease, pancreatic cancer, stress reaction, cerebrovascular disease, breast cancer, and uterine cancer.
166	2307537	NGANNOT01	Library was constructed using RNA isolated from tumorous neuroganglion tissue removed from a 9-year-old Caucasian male during a soft tissue excision of the chest wall. Pathology indicated a ganglioneuroma. Family history included asthma.
167	2440675	EOSITXT01	Library was constructed using RNA isolated from eosinophils stimulated with IL-5.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
168	2463542	THYRNOT03	Library was constructed isolated from the diseased left thyroid tissue removed from a 13-year-old Caucasian female during a complete thyroidectomy. Pathology indicated lymphocytic thyroiditis.
169	2486031	CONUTUT01	Library was constructed using RNA isolated from sigmoid mesentery tumor tissue obtained from a 61-year-old female during a total abdominal hysterectomy and bilateral salpingo-oophorectomy with regional lymph node excision. Pathology indicated a metastatic grade 4 malignant mixed mullerian tumor present in the sigmoid mesentery at two sites.
170	2493052	ADRETUT05	Library was constructed using RNA isolated from adrenal tumor tissue removed from a 52-year-old Caucasian female during a unilateral adrenalectomy. Pathology indicated a pheochromocytoma.
171	2512074	CONUTUT01	Library was constructed using RNA isolated from sigmoid mesentery tumor tissue obtained from a 61-year-old female during a total abdominal hysterectomy and bilateral salpingo-oophorectomy with regional lymph node excision. Pathology indicated a metastatic grade 4 malignant mixed mullerian tumor present in the sigmoid mesentery at two sites.
172	2646274	LUNGTUT11	Library was constructed using RNA isolated from lung tumor tissue removed from the right lower lobe of a 57-year-old Caucasian male during a segmental lung resection. Pathology indicated an infiltrating grade 4 squamous cell carcinoma. Multiple intrapulmonary peribronchial lymph nodes showed metastatic squamous cell carcinoma. Patient history included a benign brain neoplasm and tobacco abuse. Family history included spinal cord cancer, type II diabetes, cerebrovascular disease, and malignant prostate neoplasm.
173	2672566	KIDNNOT19	Library was constructed using RNA isolated from kidney tissue removed a 65-year-old Caucasian male during an exploratory laparotomy and nephroureterectomy. Patient history included malignant melanoma of the abdominal skin, benign neoplasm of colon, cerebrovascular disease, and umbilical hernia. Family history included cerebrovascular disease, prostate cancer, myocardial infarction, and atherosclerotic coronary artery disease.
174	2689674	LUNGNOT23	Library was constructed using RNA isolated from left lobe lung tissue removed from a 58-year-old Caucasian male. Patient history included soft tissue cancer, secondary cancer of the lung, prostate cancer, and an acute duodenal ulcer with hemorrhage. Family history included prostate cancer, breast cancer, and acute leukemia.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
175	2703282	OVARTUT10	Library was constructed using RNA isolated from ovarian tumor tissue removed from the left ovary of a 58-year-old Caucasian female during a total abdominal hysterectomy, removal of a solitary ovary, and repair of inguinal hernia. Pathology indicated a metastatic grade 3 adenocarcinoma of colonic origin, forming a partially cystic and necrotic tumor mass in the left ovary, and an adenocarcinoma of colonic origin, forming a nodule in the left mesovarium. A single intramural leiomyoma was identified in the myometrium. The cervix showed mild chronic cystic cervicitis. Patient history included benign hypertension, follicular cyst of the ovary, colon cancer, benign colon neoplasm, and osteoarthritis. Family history included emphysema, myocardial infarction, atherosclerotic coronary artery disease, benign hypertension, and hyperlipidemia.
176	2738293	OVARNOT09	Library was constructed using RNA isolated from ovarian tissue removed from a 28-year-old Caucasian female during a vaginal hysterectomy and removal of the fallopian tubes and ovaries. Pathology indicated multiple follicular cysts ranging in size from 0.4 to 1.5 cm in the right and left ovaries, chronic cervicitis and squamous metaplasia of the cervix, and endometrium in weakly proliferative phase. Family history included benign hypertension, hyperlipidemia, and atherosclerotic coronary artery disease.
177	2772776	PANCNOT15	Library was constructed using RNA isolated from diseased pancreatic tissue removed from a 15-year-old Caucasian male during an exploratory laparotomy with distal pancreatectomy and total splenectomy. Pathology indicated islet cell hyperplasia. Family history included prostate cancer and cardiovacular disease.
178	2774476	PANCNOT15	Library was constructed using RNA isolated from diseased pancreatic tissue removed from a 15-year-old Caucasian male during an exploratory laparotomy with distal pancreatectomy and total splenectomy. Pathology indicated islet cell hyperplasia. Family history included prostate cancer and cardiovacular disease.
179	2804624	BLADTUT08	Library was constructed using RNA isolated from bladder tumor tissue removed from a 72-year-old Caucasian male during a radical cystectomy and prostatectomy. Pathology indicated an invasive grade 3 (of 3) transitional cell carcinoma in the right bladder base. Patient history included pure hypercholesterolemia and tobacco abuse. Family history included cerebrovascular disease, brain cancer, and myocardial infarction.
180	2848225	BRSTTUT13	Library was constructed using RNA isolated from breast tumor tissue removed from the right breast of a 46-year-old Caucasian female during a unilateral extended simple mastectomy with breast reconstruction. Pathology indicated an invasive grade 3 adenocarcinoma, ductal type with apocrine features and greater than 50% intraductal component. Patient history included breast cancer.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
181	2882241	UTRSTUT05	Library was constructed using RNA isolated from uterine tumor tissue removed from a 41-year-old Caucasian female during a vaginal hysterectomy with dilation and curettage. Pathology indicated uterine leiomyoma. The endometrium was secretory and contained fragments of endometrial polyps. Benign endo- and ectocervical mucosa were identified in the endocervix. Patient history included a ventral hernia and a benign ovarian neoplasm.
182	2939011	THYMFET02	Library was constructed using RNA isolated from thymus tissue removed from a Caucasian female fetus, who died at 17 weeks' gestation from anencephalus.
183	2947188	BRAITUT23	Library was constructed using RNA isolated from left posterior brain tumor tissue removed from a 36-year-old male during a cerebral meninges lesion excision. Pathology indicated meningioma. Family history included malignant skin melanoma, atherosclerotic coronary artery disease, repair of unspecified vessel, hyperlipidemia, Huntington's chorea, and rheumatoid arthritis.
184	3094001	BRSTNOT19	Library was constructed using RNA isolated from breast tissue removed from a 67-year-old Caucasian female during a unilateral extended simple mastectomy. Patient history included depressive disorder and benign large bowel neoplasm. Family history included cerebrovascular disease, benign hypertension, congestive heart failure, and lung cancer.
185	3110061	BRSTNOT19	Library was constructed using RNA isolated from breast tissue removed from a 67-year-old Caucasian female during a unilateral extended simple mastectomy. Patient history included depressive disorder, benign large bowel neoplasm, and hemorrhoids. Family history included cerebrovascular and cardiovascular disease and lung cancer.
186	3146614	BRSTTUT15	Library was constructed using RNA isolated from breast tumor tissue removed from a 46-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated invasive grade 3, nuclear grade 2 adenocarcinoma, ductal type. An intraductal carcinoma component, non-comedo, comprised approximately 50% of the neoplasm, including the lactiferous ducts. Angiolymphatic involvement was present. Metastatic adenocarcinoma was present in 7 of 10 axillary lymph nodes. The largest nodal metastasis measured 3 cm, and focal extracapsular extension was identified. Family history included atherosclerotic coronary artery disease, type II diabetes, cerebrovascular disease, and depression.
187	3295381	PENCNOT06	Library was constructed using RNA isolated from penis corpora cavernosa tissue removed from a 3-year-old Black male.
188	3364774	TLYJINT01	Library was constructed using RNA isolated from a Jurkat cell line derived from the T cells of a male. The cells were treated for 18 hours with 50 ng/ml phorbol ester (PMA) and 1 micromolar calcium ionophore. Patient history included acute T-cell leukemia.

Table 4 (cont.)

SEQ ID NO:	Nucleotide	Library	Library Description
189	3397777	PROSBPT02	Library was constructed using RNA isolated from diseased prostate tissue removed from a 65-year-old Caucasian male during a radical prostatectomy. Pathology indicated benign prostatic hyperplasia (BPH). One (of 7) right pelvic lymph nodes was positive for metastatic adenocarcinoma. The patient presented with induration and elevated prostate specific antigen (PSA). Patient history included a benign neoplasm of the large bowel and benign hypertension.
190	3403046	ESOGNOT03	Library was constructed using RNA isolated from esophageal tissue obtained from a 53-year-old Caucasian male during a partial esophagectomy, proximal gastrectomy, and regional lymph node biopsy. Patient history included membranous nephritis, hyperlipidemia, benign hypertension, and anxiety state. Previous surgeries included an adenotonsillectomy. Family history included cirrhosis, abdominal aortic aneurysm rupture, breast cancer, myocardial infarction, and atherosclerotic coronary artery disease.
191	3538506	SEMVNOT04	Library was constructed using RNA isolated from seminal vesicle tissue removed from a 61-year-old Caucasian male during a radical prostatectomy. Pathology for the associated tumor tissue indicated adenocarcinoma, Gleason grade 3+3. The patient presented with induration, hyperplasia of the prostate, and elevated prostate specific antigen. Patient history included renal failure, osteoarthritis, left renal artery stenosis, thrombocytopenia, hyperlipidemia, and hepatitis C (carrier). Family history included benign hypertension.
192	3575519	BRONNOT01	Library was constructed using RNA isolated from bronchial tissue removed from a 15-year-old Caucasian male.
193	3598694	FIBPNOT01	Library was constructed using RNA isolated from fibroblasts of the prostate stroma removed from a male fetus, who died after 26 weeks' gestation.
194	3638819	LUNGNOT30	Library was constructed using RNA isolated from lung tissue removed from a Caucasian male fetus, who died from Patau's syndrome (trisomy 13) at 20-weeks' gestation.
195	3717139	PENCNOT10	Library was constructed using RNA isolated from penis left corpora cavernosa tissue removed from a male.
196	3892962	BRSTTUT16	Library was constructed using RNA isolated from breast tumor tissue removed from a 43-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated recurrent grade 4, nuclear grade 3, ductal carcinoma. Angiolymphatic space invasion was identified. Left breast needle biopsy indicated grade 4 ductal adenocarcinoma. Paraffin embedded tissue was estrogen positive. Patient history included breast cancer and deficiency anemia. Family history included cervical cancer.

Table 4 (cont.)

SEQ ID NO:	Nucleotide	Library	Library Description
197	4153521	MUSLTMT01	Library was constructed using RNA isolated from glossal muscle tissue removed from a 41-year-old Caucasian female during partial glossectomy. Pathology for the matched tumor tissue indicated invasive grade 3, squamous cell carcinoma forming an ulcerated mass of the tongue. The tumor infiltrated superficially into muscle. One high lymph node contained a necrotizing granuloma. The patient presented with a complicated open wound of the tongue. Patient history included obesity, unspecified nasal and sinus disease, and normal delivery. Patient medications included Premarin, Hydrocodone, and Equate nasal spray. Family history included benign hypertension, atherosclerotic coronary artery disease, upper lobe lung cancer, type II diabetes, hyperlipidemia, and cirrhosis of the liver.
198	4585038	OVARNOT13	Library was constructed using RNA isolated from left ovary tissue removed from a 47-year-old Caucasian female during a vaginal hysterectomy with bilateral salpingo-oophorectomy, and dilation and curettage. Pathology for the associated tumor tissue indicated a single intramural leiomyoma. The endometrium was in the secretory phase. The patient presented with metrorrhagia. Patient history included hyperlipidemia and benign hypertension. Family history included colon cancer, benign hypertension, atherosclerotic coronary artery disease, and breast cancer.
199	4674640	NOSEDIT02	Library was constructed using RNA isolated from nasal polyp tissue.
200	4676066	NOSEDIT02	Library was constructed using RNA isolated from nasal polyp tissue.
201	4830687	BRAVTXT03	Library was constructed using RNA isolated from treated astrocytes removed from the brain of a female fetus who died after 22 weeks' gestation. The cells were treated with tumor necrosis factor-alpha (TNF) and interleukin 1 (IL-1), 10ng/ml each for 24 hours.
202	4880891	UTRMTMT01	Library was constructed using RNA isolated from myometrial tissue removed from a 45-year-old Caucasian female during vaginal hysterectomy and bilateral salpingo-oophorectomy. Pathology for the matched tumor tissue indicated multiple (23) subserosal, intramural, and submucosal leiomyomata. The endometrium was in proliferative phase. The right ovary contained an old corpus luteum. The patient presented with stress incontinence. Patient history included normal delivery. Patient medications included Motrin, iron sulfate, Premarin, prednisone, Tylenol #3, and Colace. Family history included cerebrovascular disease, depression, and atherosclerotic coronary artery disease.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
203	4909754	THYMDIT01	Library was constructed using RNA isolated from diseased thymus tissue removed from a 16-year-old Caucasian female during a total excision of thymus and regional lymph node excision. Pathology indicated thymic follicular hyperplasia. The right lateral thymus showed reactive lymph nodes. A single reactive lymph node was also identified at the inferior thymus margin. The patient presented with myasthenia gravis, malaise, fatigue, dysphagia, severe muscle weakness, and prominent eyes. Patient history included frozen face muscles. Family history included depression, hepatitis B, myocardial infarction, atherosclerotic coronary artery disease, leukemia, multiple sclerosis, and lupus.
204	4911931	THYMDIT01	Library was constructed using RNA isolated from diseased thymus tissue removed from a 16-year-old Caucasian female during a total excision of thymus and regional lymph node excision. Pathology indicated thymic follicular hyperplasia. The right lateral thymus showed reactive lymph nodes. A single reactive lymph node was also identified at the inferior thymus margin. The patient presented with myasthenia gravis, malaise, fatigue, dysphagia, severe muscle weakness, and prominent eyes. Patient history included frozen face muscles. Family history included depression, hepatitis B, myocardial infarction, atherosclerotic coronary artery disease, leukemia, multiple sclerosis, and lupus.
205	4920433	TESTNOT11	Library was constructed using RNA isolated from testicular tissue removed from a 16-year-old Caucasian male who died from hanging.
206	5042113	COLHTUT01	Library was constructed using RNA isolated from colon tumor tissue removed from the hepatic flexure of a 55-year-old Caucasian male during right hemicolectomy, incidental appendectomy, and permanent colostomy. Pathology indicated invasive grade 3 adenocarcinoma. Patient history included benign hypertension, anxiety, abnormal blood chemistry, blepharitis, heart block, osteoporosis, acne, and hyperplasia of prostate. Family history included prostate cancer, acute myocardial infarction, stroke, and atherosclerotic coronary artery disease.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
207	5083853	LNOGTUT01	Library was constructed using RNA isolated from gastric lymph node tumor tissue removed from a 61-year-old Caucasian male during proximal gastrectomy and partial esophagectomy. Pathology indicated invasive grade 3 adenocarcinoma forming an ulcerated, plaque-like mass situated at the lower esophagus just proximal to the gastroesophageal junction, with partial involvement of cardiac mucosa. Metastatic adenocarcinoma was identified in 2 of 3 paraesophageal and 9 of 14 paragastric lymph nodes with perinodal extension to form grossly matted nodes. The paraesophageal lymph node contained metastatic grade 3 adenocarcinoma with perinodal extension. Tissue from the mesentery showed dense fibrosis with chronic inflammation and focal calcification. Patient history included a benign colon neoplasm and hyperlipidemia. Family history included type II diabetes, accessory sinus cancer, atherosclerotic coronary artery disease, and acute myocardial infarction.
208	5283981	TESTNON04	This normalized testis tissue library was constructed from 6.48 million independent clones from a pool of two testicular libraries. Starting RNA was made from testicular tissue removed from a 16-year-old Caucasian male who died from hanging. The library was normalized in two rounds using conditions adapted from Soares et al., PNAS (1994) 91:9228 and Bonaldo et al. except that a significantly longer (48-hours/round) reannealing hybridization was used.
209	5510549	BRADDIR01	Library was constructed using RNA isolated from diseased choroid plexus tissue of the lateral ventricle removed from the brain of a 57-year-old Caucasian male, who died from a cerebrovascular accident. Patient history included Huntington's disease and emphysema.
210	5544862	BRADDIR01	Library was constructed using RNA isolated from diseased choroid plexus tissue of the lateral ventricle removed from the brain of a 57-year-old Caucasian male, who died from a cerebrovascular accident. Patient history included Huntington's disease and emphysema.
211	5573394	TLYMNOT08	Library was constructed using RNA isolated from anergic allogenic T-lymphocyte tissue removed from an adult (40-50-year-old) Caucasian male. The cells were incubated for 3 days in the presence of OKT3 mAb (1 microgram/mlOKT3) and 5% human serum.
212	5850840	FIBAUNT02	Library was constructed using RNA isolated from untreated aortic adventitial fibroblasts removed from a 65-year-old Caucasian female.

Table 4 (cont.)

Nucleotide SEQ ID NO:		Library	Library Description
213	5942936	COLADIT05	Library was constructed using RNA isolated from diseased ascending colon tissue removed from a 32-year-old Caucasian male during a total intra-abdominal colectomy, abdominal-perineal rectal resection, and temporary ileostomy. Pathology indicated chronic ulcerative colitis extending in a continuous fashion from the mid-portion of the ascending colon to the rectum. This was characterized by crypt abscess formation and inflammation confined to the mucosa and submucosa. The terminal ileum exhibited ileitis and the rectal mucosa showed crypt abscess formation. The patient presented with ulcerative colitis and blood in the stools. Patient history included tobacco use. Patient medications included Imuran, prednisone, sulfasalazine, and azathioprine. Family history included ulcerative colitis, malignant breast neoplasm and acute myocardial infarction.
214	5951431	LIVRTUN04	This normalized library was constructed from 1.72 million independent clones from an untreated C3A liver tumor library. C3A is a derivative of Hep G2, a cell line derived from a hepatoblastoma removed from a 15-year-old Caucasian male. The library was normalized in two rounds using conditions adapted from Soares et al., PNAS (1994) 91:9228-9232 and Bonaldo et al., Genome Research 6 (1996):791, except that a significantly longer (48 hours/round) reannealing hybridization was used.

Table 5

Program	Description	Reference	Parameter Threshold
ABI FACTURA	A program that removes vector sequences and masks ambiguous bases in nucleic acid sequences.	Applied Biosystems, Foster City, CA.	
ABI/PARACEL FDF	A Fast Data Finder useful in comparing and annotating amino acid or nucleic acid sequences.	Applied Biosystems, Foster City, CA; Paracel Inc., Pasadena, CA.	Mismatch <50%
ABI AutoAssembler	A program that assembles nucleic acid sequences.	Applied Biosystems, Foster City, CA.	
BLAST	A Basic Local Alignment Search Tool useful in sequence similarity search for amino acid and nucleic acid sequences. BLAST includes five functions: blastp, blastn, blastx, tblastn, and tblastx.	Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410; Altschul, S.F. et al. (1997) Nucleic Acids Res. 25:3389-3402.	*ESTs:* Probability value= 1.0E-8 or less *Full Length sequences*: Probability value= 1.0E-10 or less
FASTA	A Pearson and Lipman algorithm that searches for similarity between a query sequence and a group of sequences of the same type. FASTA comprises as least five functions: fasta, tfasta, fastx, tfastx, and ssearch.	Pearson, W.R. and D.J. Lipman (1988) Proc. Natl. Acad Sci. USA 85:2444-2448; Pearson, W.R. (1990) Methods Enzymol. 183:63-98; and Smith, T.F. and M.S. Waterman (1981) Adv. Appl. Math. 2:482-489.	*ESTs:* fasta E value=1.06E-6 *Assembled ESTs*: fasta Identity= 95% or greater and Match length=200 bases or greater; fastx E value=1.0E-8 or less *Full Length sequences:* fastx score=100 or greater
BLIMPS	A BLocks IMProved Searcher that matches a sequence against those in BLOCKS, PRINTS, DOMO, PRODOM, and PFAM databases to search for gene families, sequence homology, and structural fingerprint regions.	Henikoff, S. and J.G. Henikoff (1991) Nucleic Acids Res. 19:6565-6572; Henikoff, J.G. and S. Henikoff (1996) Methods Enzymol. 266:88-105; and Attwood, T.K. et al. (1997) J. Chem. Inf. Comput. Sci. 37:417-424.	Score=1000 or greater; Ratio of Score/Strength = 0.75 or larger; and, if applicable, Probability value= 1.0E-3 or less
HMMER	An algorithm for searching a query sequence against hidden Markov model (HMM)-based databases of protein family consensus sequences, such as PFAM.	Krogh, A. et al. (1994) J. Mol. Biol. 235:1501-1531; Sonnhammer, E.L.L. et al. (1988) Nucleic Acids Res. 26:320-322; Durbin, R. et al. (1998) Our World View, in a Nutshell, Cambridge Univ. Press, pp. 1-350.	Score=10-50 bits for PFAM hits, depending on individual protein families

Table 5 (cont.)

Program	Description	Reference	Parameter Threshold
ProfileScan	An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.	Gribskov, M. et al. (1988) CABIOS 4:61-66; Gribskov, M. et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221.	Normalized quality score≥GCG-specified "HIGH" value for that particular Prosite motif. Generally, score=1.4-2.1.
Phred	A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.	Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.	
Phrap	A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences.	Smith, T.F. and M.S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M.S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA.	Score= 120 or greater; Match length= 56 or greater
Consed	A graphical tool for viewing and editing Phrap assemblies.	Gordon, D. et al. (1998) Genome Res. 8:195-202.	
SPScan	A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.	Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12:431-439.	Score=3.5 or greater
Motifs	A program that searches amino acid sequences for patterns that matched those defined in Prosite.	Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.	

What is claimed is:

1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-107,

b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-107,

c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107, and

d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-107.

2. An isolated polypeptide of claim 1 selected from the group consisting of SEQ ID NO:1-107.

3. An isolated polynucleotide encoding a polypeptide of claim 1.

4. An isolated polynucleotide encoding a polypeptide of claim 2.

5. An isolated polynucleotide of claim 4 selected from the group consisting of SEQ ID NO:108-214.

6. A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.

7. A cell transformed with a recombinant polynucleotide of claim 6.

8. A transgenic organism comprising a recombinant polynucleotide of claim 6.

9. A method for producing a polypeptide of claim 1, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and

b) recovering the polypeptide so expressed.

10. An isolated antibody which specifically binds to a polypeptide of claim 1.

11. An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214,

b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:108-214,

c) a polynucleotide sequence complementary to a),

d) a polynucleotide sequence complementary to b), and

e) an RNA equivalent of a)-d).

12. An isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of claim 11.

13. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

14. A method of claim 13, wherein the probe comprises at least 60 contiguous nucleotides.

15. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

16. A composition comprising an effective amount of a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

17. A composition of claim 16, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-107.

18. A method for treating a disease or condition associated with decreased expression of functional TRFX, comprising administering to a patient in need of such treatment the composition of claim 16.

19. A method for screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting agonist activity in the sample.

20. A composition comprising an agonist compound identified by a method of claim 19 and a pharmaceutically acceptable excipient.

21. A method for treating a disease or condition associated with decreased expression of functional TRFX, comprising administering to a patient in need of such treatment a composition of claim 20.

22. A method for screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting antagonist activity in the sample.

23. A composition comprising an antagonist compound identified by a method of claim 22 and a pharmaceutically acceptable excipient.

24. A method for treating a disease or condition associated with overexpression of functional TRFX, comprising administering to a patient in need of such treatment a composition of claim 23.

25. A method of screening for a compound that specifically binds to the polypeptide of claim

1, said method comprising the steps of:

a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

26. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, said method comprising:

a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,

b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

27. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

28. A method for assessing toxicity of a test compound, said method comprising:

a) treating a biological sample containing nucleic acids with the test compound;

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;

c) quantifying the amount of hybridization complex; and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

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Tyr Arg Ser Glu Glu Lys Arg Lys His Leu Thr Val Pro Lys Glu
               350                 355                 360
Asn Lys Ile Pro Thr Val Ser Lys Asn His Ala His Glu His Phe
               365                 370                 375
Leu Asp Leu Gly Glu Ser Lys Lys Gln Gln Thr Asn Gln His Asn
               380                 385                 390
Tyr Arg Thr Arg Ser Ala Leu Glu Glu Thr Pro Arg Pro Ser Glu
               395                 400                 405
```

Glu Ile Glu Asn Gly Ser Ser Ser Ser Asp Glu Gly Glu Val Val
410 415 420
Ala Val Ser Gly Gly Thr Ser Glu Glu Glu Glu Arg Ala Trp His
425 430 435
Ser Asp Gly Ser Ser Ser Asp Tyr Ser Ser Asp Tyr Ser Asp Trp
440 445 450
Thr Ala Asp Ala Gly Ile Asn Leu Gln Pro Pro Lys Lys Val Pro
455 460 465
Lys Asn Lys Thr Lys Lys Ala Glu Ser Ser Ser Asp Glu Glu Glu
470 475 480
Glu Ser Glu Lys Gln Lys Gln Lys Gln Ile Lys Lys Glu Lys Lys
485 490 495
Lys Val Asn Glu Glu Lys Asp Gly Pro Ile Ser Pro Lys Lys Lys
500 505 510
Lys Pro Lys Glu Arg Lys Gln Lys Arg Leu Ala Val Gly Glu Leu
515 520 525
Thr Glu Asn Gly Leu Thr Leu Glu Glu Trp Leu Pro Ser Thr Trp
530 535 540
Ile Thr Asp Thr Ile Pro Arg Arg Cys Pro Phe Val Pro Gln Met
545 550 555
Gly Asp Glu Val Tyr Tyr Phe Arg Gln Gly His Glu Ala Tyr Val
560 565 570
Glu Met Ala Arg Lys Asn Lys Ile Tyr Ser Ile Asn Pro Lys Lys
575 580 585
Gln Pro Trp His Lys Met Glu Leu Arg Glu Gln Glu Leu Met Lys
590 595 600
Ile Val Gly Ile Lys Tyr Glu Val Gly Leu Pro Thr Leu Cys Cys
605 610 615
Leu Lys Leu Ala Phe Leu Asp Pro Asp Thr Gly Lys Leu Thr Gly
620 625 630
Gly Ser Phe Thr Met Lys Tyr His Asp Met Pro Asp Val Ile Asp
635 640 645
Phe Leu Val Leu Arg Gln Gln Phe Asp Asp Ala Lys Tyr Arg Arg
650 655 660
Trp Asn Ile Gly Asp Arg Phe Arg Ser Val Ile Asp Asp Ala Trp
665 670 675
Trp Phe Gly Thr Ile Glu Ser Gln Glu Pro Leu Gln Leu Glu Tyr
680 685 690
Pro Asp Ser Leu Phe Gln Cys Tyr Asn Val Cys Trp Asp Asn Gly
695 700 705
Asp Thr Glu Lys Val Ser Pro Trp Asp Met Glu Leu Ile Pro Asn
710 715 720
Asn Ala Val Phe Pro Glu Glu Leu Gly Thr Ser Val Pro Leu Thr
725 730 735
Asp Gly Glu Cys Arg Ser Leu Ile Tyr Lys Pro Leu Asp Gly Glu
740 745 750
Trp Gly Thr Asn Pro Arg Asp Glu Glu Cys Glu Arg Ile Val Ala
755 760 765
Gly Ile Asn Gln Leu Met Thr Leu Asp Ile Ala Ser Ala Phe Val
770 775 780
Ala Pro Val Asp Leu Gln Ala Tyr Pro Met Tyr Cys Thr Val Val
785 790 795
Ala Tyr Pro Thr Asp Leu Ser Thr Ile Lys Gln Arg Leu Glu Asn
800 805 810
Arg Phe Tyr Arg Arg Val Ser Ser Leu Met Trp Glu Val Arg Tyr
815 820 825
Ile Glu His Asn Thr Arg Thr Phe Asn Glu Pro Gly Ser Pro Ile
830 835 840
Val Lys Ser Ala Lys Phe Val Thr Asp Leu Leu Leu His Phe Ile
845 850 855
Lys Asp Gln Thr Cys Tyr Asn Ile Ile Pro Leu Tyr Asn Ser Met
860 865 870
Lys Lys Lys Val Leu Ser Asp Ser Glu Asp Glu Glu Lys Asp Ala

875 880 885
Asn Val Pro Gly Thr Ser Thr Arg Lys Arg Lys Asp His Gln Pro
890 895 900
Arg Arg Arg Leu Arg Asn Arg Ala Gln Ser Tyr Asp Ile Gln Ala
905 910 915
Trp Lys Lys Gln Cys Glu Glu Leu Leu Asn Leu Ile Phe Gln Cys
920 925 930
Glu Asp Ser Glu Pro Phe Arg Gln Pro Val Asp Leu Leu Glu Tyr
935 940 945
Pro Asp Tyr Arg Asp Ile Ile Asp Thr Pro Met Asp Phe Ala Thr
950 955 960
Val Arg Glu Thr Leu Glu Ala Gly Asn Tyr Glu Ser Pro Met Glu
965 970 975
Leu Cys Lys Asp Val Arg Leu Ile Phe Ser Asn Ser Lys Ala Tyr
980 985 990
Thr Pro Ser Lys Arg Ser Arg Ile Tyr Ser Met Ser Leu Arg Leu
995 1000 1005
Ser Ala Phe Phe Glu Glu His Ile Ser Ser Val Leu Ser Asp Tyr
1010 1015 1020
Lys Ser Ala Leu Arg Phe His Lys Arg Asn Thr Ile Thr Lys Arg
1025 1030 1035
Arg Lys Lys Arg Asn Arg Ser Ser Ser Val Ser Ser Ser Ala Ala
1040 1045 1050
Ser Ser Pro Glu Arg Lys Lys Arg Ile Leu Lys Pro Gln Leu Lys
1055 1060 1065
Ser Glu Ser Ser Thr Ser Ala Phe Ser Thr Pro Thr Arg Ser Ile
1070 1075 1080
Pro Pro Arg His Asn Ala Ala Gln Ile Asn Gly Lys Thr Glu Ser
1085 1090 1095
Ser Ser Val Val Arg Thr Arg Ser Asn Arg Val Val Val Asp Pro
1100 1105 1110
Val Val Thr Glu Gln Pro Ser Thr Ser Ser Ala Ala Lys Thr Phe
1115 1120 1125
Ile Thr Lys Ala Asn Ala Ser Ala Ile Pro Gly Lys Thr Ile Leu
1130 1135 1140
Glu Asn Ser Val Lys His Ser Lys Ala Leu Asn Thr Leu Ser Ser
1145 1150 1155
Pro Gly Gln Ser Ser Phe Ser His Gly Thr Arg Asn Asn Ser Ala
1160 1165 1170
Lys Glu Asn Met Glu Lys Glu Lys Pro Val Lys Arg Lys Met Lys
1175 1180 1185
Ser Ser Val Leu Pro Lys Ala Ser Thr Leu Ser Lys Ser Ser Ala
1190 1195 1200
Val Ile Glu Gln Gly Asp Cys Lys Asn Asn Ala Leu Val Pro Gly
1205 1210 1215
Thr Ile Gln Val Asn Gly His Gly Gly Gln Pro Ser Lys Leu Val
1220 1225 1230
Lys Arg Gly Pro Gly Arg Lys Pro Lys Val Glu Val Asn Thr Asn
1235 1240 1245
Ser Gly Glu Ile Ile His Lys Lys Arg Gly Arg Lys Pro Lys Lys
1250 1255 1260
Leu Gln Tyr Ala Lys Pro Glu Asp Leu Glu Gln Asn Asn Val His
1265 1270 1275
Pro Ile Arg Asp Glu Val Leu Pro Ser Ser Thr Cys Asn Phe Leu
1280 1285 1290
Ser Glu Thr Asn Asn Val Lys Glu Asp Leu Leu Gln Lys Lys Asn
1295 1300 1305
Arg Gly Gly Arg Lys Pro Lys Arg Lys Met Lys Thr Gln Lys Leu
1310 1315 1320
Asp Ala Asp Leu Leu Val Pro Ala Ser Val Lys Val Leu Arg Arg
1325 1330 1335
Ser Asn Arg Lys Lys Ile Asp Asp Pro Ile Asp Glu Glu Glu Glu
1340 1345 1350

```
Phe Glu Glu Leu Lys Gly Ser Glu Pro His Met Arg Thr Arg Asn
                1355                1360                1365
Gln Gly Arg Arg Thr Ala Phe Tyr Asn Glu Asp Asp Ser Glu Glu
                1370                1375                1380
Glu Gln Arg Gln Leu Leu Phe Glu Asp Thr Ser Leu Thr Phe Gly
                1385                1390                1395
Thr Ser Ser Arg Gly Arg Val Arg Lys Leu Thr Glu Lys Ala Lys
                1400                1405                1410
Ala Asn Leu Ile Gly Trp
                1415

<210> 5
<211> 426
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 402386CD1

<400> 5
Met Asp Ser Val Ala Phe Glu Asp Val Ala Val Asn Phe Thr Gln
  1               5                   10                  15
Glu Glu Trp Ala Leu Leu Ser Pro Ser Gln Lys Asn Leu Tyr Arg
                 20                   25                  30
Asp Val Thr Leu Glu Thr Phe Arg Asn Leu Ala Ser Val Gly Ile
                 35                   40                  45
Gln Trp Lys Asp Gln Asp Ile Glu Asn Leu Tyr Gln Asn Leu Gly
                 50                   55                  60
Ile Lys Leu Arg Ser Leu Val Glu Arg Leu Cys Gly Arg Lys Glu
                 65                   70                  75
Gly Asn Glu His Arg Glu Thr Phe Ser Gln Ile Pro Asp Cys His
                 80                   85                  90
Leu Asn Lys Lys Ser Gln Thr Gly Val Lys Pro Cys Lys Cys Ser
                 95                  100                 105
Val Cys Gly Lys Val Phe Leu Arg His Ser Phe Leu Asp Arg His
                110                  115                 120
Met Arg Ala His Ala Gly His Lys Arg Ser Glu Cys Gly Gly Glu
                125                  130                 135
Trp Arg Glu Thr Pro Arg Lys Gln Lys Gln His Gly Lys Ala Ser
                140                  145                 150
Ile Ser Pro Ser Ser Gly Ala Arg Arg Thr Val Thr Pro Thr Arg
                155                  160                 165
Lys Arg Pro Tyr Glu Cys Lys Val Cys Gly Lys Ala Phe Asn Ser
                170                  175                 180
Pro Asn Leu Phe Gln Ile His Gln Arg Thr His Thr Gly Lys Arg
                185                  190                 195
Ser Tyr Lys Cys Arg Glu Ile Val Arg Ala Phe Thr Val Ser Ser
                200                  205                 210
Phe Phe Arg Lys His Gly Lys Met His Thr Gly Glu Lys Arg Tyr
                215                  220                 225
Glu Cys Lys Tyr Cys Gly Lys Pro Ile Asp Tyr Pro Ser Leu Phe
                230                  235                 240
Gln Ile His Val Arg Thr His Ala Gly Glu Lys Pro Tyr Lys Cys
                245                  250                 255
Lys Gln Cys Gly Lys Ala Phe Ile Ser Ala Gly Tyr Leu Arg Thr
                260                  265                 270
His Glu Ile Arg Ser His Ala Leu Glu Lys Ser His Gln Cys Gln
                275                  280                 285
Glu Cys Gly Lys Lys Leu Ser Cys Ser Ser Ser Leu His Arg His
                290                  295                 300
Glu Arg Thr His Ser Gly Gly Lys Leu Tyr Glu Cys Gln Lys Cys
                305                  310                 315
```

```
Ala Lys Val Phe Arg Cys Pro Thr Ser Leu Gln Ala His Glu Arg
                320                 325                 330
Ala His Thr Gly Glu Arg Pro Tyr Glu Cys Asn Lys Cys Gly Lys
                335                 340                 345
Thr Phe Asn Tyr Pro Ser Cys Phe Arg Arg His Lys Lys Thr His
                350                 355                 360
Ser Gly Glu Lys Pro Tyr Glu Cys Thr Arg Cys Gly Lys Ala Phe
                365                 370                 375
Gly Trp Cys Ser Ser Leu Arg Arg His Glu Met Thr His Thr Gly
                380                 385                 390
Glu Lys Pro Phe Asp Cys Lys Gln Cys Gly Lys Val Phe Thr Phe
                395                 400                 405
Ser Asn Tyr Leu Ser Leu Leu Gln Ala Arg Ala Asp Met Pro Gly
                410                 415                 420
Trp Phe Phe Val Phe Trp
                425
```

<210> 6
<211> 686
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 456487CD1

<400> 6

```
Met Gly Asn Ile Leu Thr Cys Arg Val His Pro Ser Val Ser Leu
 1               5                  10                  15
Glu Phe Asp Gln Gln Gln Gly Ser Val Cys Pro Ser Glu Ser Glu
                20                  25                  30
Ile Tyr Glu Ala Gly Ala Gly Asp Arg Met Ala Gly Ala Pro Met
                35                  40                  45
Ala Ala Ala Val Gln Pro Ala Glu Val Thr Val Glu Val Gly Glu
                50                  55                  60
Asp Leu His Met His His Val Arg Asp Arg Glu Met Pro Glu Ala
                65                  70                  75
Leu Glu Phe Asn Leu Ser Ala Asn Pro Glu Ala Ser Thr Ile Phe
                80                  85                  90
Gln Arg Asn Ser Gln Thr Asp Ala Leu Glu Phe Asn Pro Ser Ala
                95                  100                 105
Asn Pro Glu Ala Ser Thr Ile Phe Gln Arg Asn Ser Gln Thr Asp
                110                 115                 120
Val Val Glu Ile Arg Arg Ser Asn Cys Thr Asn His Val Ser Thr
                125                 130                 135
Val Arg Phe Ser Gln Gln Tyr Ser Leu Cys Ser Thr Ile Phe Leu
                140                 145                 150
Asp Asp Ser Thr Ala Ile Gln His Tyr Leu Thr Met Thr Ile Ile
                155                 160                 165
Ser Val Thr Leu Glu Ile Pro His His Ile Thr Gln Arg Asp Ala
                170                 175                 180
Asp Arg Ser Leu Ser Ile Pro Asp Glu Gln Leu His Ser Phe Ala
                185                 190                 195
Val Ser Thr Val His Ile Met Lys Lys Arg Asn Gly Gly Gly Ser
                200                 205                 210
Leu Asn Asn Tyr Ser Ser Ser Ile Pro Ser Thr Pro Ser Thr Ser
                215                 220                 225
Gln Glu Asp Pro Gln Phe Ser Val Pro Pro Thr Ala Asn Thr Pro
                230                 235                 240
Thr Pro Val Cys Lys Arg Ser Met Arg Trp Ser Asn Leu Phe Thr
                245                 250                 255
Ser Glu Lys Gly Ser Asp Pro Asp Lys Glu Arg Lys Ala Pro Glu
                260                 265                 270
```

Asn His Ala Asp Thr Ile Gly Ser Gly Arg Ala Ile Pro Ile Lys
275 280 285
Gln Gly Met Leu Leu Lys Arg Ser Gly Lys Trp Leu Lys Thr Trp
290 295 300
Lys Lys Lys Tyr Val Thr Leu Cys Ser Asn Gly Met Leu Thr Tyr
305 310 315
Tyr Ser Ser Leu Gly Asp Tyr Met Lys Asn Ile His Lys Lys Glu
320 325 330
Ile Asp Leu Gln Thr Ser Thr Ile Lys Val Pro Gly Lys Trp Pro
335 340 345
Ser Leu Ala Thr Ser Ala Cys Thr Pro Ile Ser Ser Ser Lys Ser
350 355 360
Asn Gly Leu Ser Lys Asp Met Asp Thr Gly Leu Gly Asp Ser Ile
365 370 375
Cys Phe Ser Pro Ser Ile Ser Ser Thr Thr Ser Pro Lys Leu Asn
380 385 390
Pro Pro Pro Ser Pro His Ala Asn Lys Lys Lys His Leu Lys Lys
395 400 405
Lys Ser Thr Asn Asn Phe Met Ile Val Ser Ala Thr Gly Gln Thr
410 415 420
Trp His Phe Glu Ala Thr Thr Tyr Glu Glu Arg Asp Ala Trp Val
425 430 435
Gln Ala Ile Gln Ser Gln Ile Leu Ala Ser Leu Gln Ser Cys Glu
440 445 450
Ser Ser Lys Ser Lys Ser Gln Leu Thr Ser Gln Ser Glu Ala Met
455 460 465
Ala Leu Gln Ser Ile Gln Asn Met Arg Gly Asn Ala His Cys Val
470 475 480
Asp Cys Glu Thr Gln Asn Pro Lys Trp Ala Ser Leu Asn Leu Gly
485 490 495
Val Leu Met Cys Ile Glu Cys Ser Gly Ile His Arg Ser Leu Gly
500 505 510
Thr Arg Leu Ser Arg Val Arg Ser Leu Glu Leu Asp Asp Trp Pro
515 520 525
Val Glu Leu Arg Lys Val Met Ser Ser Ile Gly Asn Asp Leu Ala
530 535 540
Asn Ser Ile Trp Glu Gly Ser Ser Gln Gly Gln Thr Lys Pro Ser
545 550 555
Glu Lys Ser Thr Arg Glu Glu Lys Glu Arg Trp Ile Arg Ser Lys
560 565 570
Tyr Glu Glu Lys Leu Phe Leu Ala Pro Leu Pro Cys Thr Glu Leu
575 580 585
Ser Leu Gly Gln Gln Leu Leu Arg Ala Thr Ala Asp Glu Asp Leu
590 595 600
Gln Thr Ala Ile Leu Leu Leu Ala His Gly Ser Arg Glu Glu Val
605 610 615
Asn Glu Thr Cys Gly Glu Gly Asp Gly Cys Thr Ala Leu His Leu
620 625 630
Ala Cys Arg Lys Gly Asn Val Val Leu Ala Gln Leu Leu Ile Trp
635 640 645
Tyr Gly Val Asp Val Met Ala Arg Asp Ala His Gly Asn Thr Ala
650 655 660
Leu Thr Tyr Ala Arg Gln Ala Ser Ser Gln Glu Cys Ile Asn Val
665 670 675
Leu Leu Gln Tyr Gly Cys Pro Asp Lys Cys Val
680 685

<210> 7
<211> 348
<212> PRT
<213> Homo sapiens

<220>

<221> misc_feature
<223> Incyte ID No: 490256CD1

<400> 7
Met Thr Thr Ala Leu Glu Pro Glu Asp Gln Lys Gly Leu Leu Ile
1 5 10 15
Ile Lys Ala Glu Asp His Tyr Trp Gly Gln Asp Ser Ser Ser Gln
20 25 30
Lys Cys Ser Pro His Arg Arg Glu Leu Tyr Arg Gln His Phe Arg
35 40 45
Lys Leu Cys Tyr Gln Asp Ala Pro Gly Pro Arg Glu Ala Leu Thr
50 55 60
Gln Leu Trp Glu Leu Cys Arg Gln Trp Leu Arg Pro Glu Cys His
65 70 75
Thr Lys Glu Gln Ile Leu Asp Leu Leu Val Leu Glu Gln Ser Leu
80 85 90
Ser Ile Leu Pro Lys Asp Leu Gln Ala Trp Val Arg Ala His His
95 100 105
Pro Glu Thr Gly Glu Glu Ala Val Thr Val Leu Glu Asp Leu Glu
110 115 120
Arg Glu Leu Asp Glu Pro Gly Lys Gln Val Pro Gly Asn Ser Glu
125 130 135
Arg Arg Asp Ile Leu Met Asp Lys Leu Ala Pro Leu Gly Arg Pro
140 145 150
Tyr Glu Ser Leu Thr Val Gln Leu His Pro Lys Lys Thr Gln Leu
155 160 165
Glu Gln Glu Ala Gly Lys Pro Gln Arg Asn Gly Asp Lys Thr Arg
170 175 180
Thr Lys Asn Glu Glu Leu Phe Gln Lys Glu Asp Met Pro Lys Asp
185 190 195
Lys Glu Phe Leu Gly Glu Ile Asn Asp Arg Leu Asn Lys Asp Thr
200 205 210
Pro Gln His Pro Lys Ser Lys Asp Ile Ile Glu Asn Glu Gly Arg
215 220 225
Ser Glu Trp Gln Gln Arg Glu Arg Arg Arg Tyr Lys Cys Asp Glu
230 235 240
Cys Gly Lys Ser Phe Ser His Ser Ser Asp Leu Ser Lys His Arg
245 250 255
Arg Thr His Thr Gly Glu Lys Pro Tyr Lys Cys Asp Glu Cys Gly
260 265 270
Lys Ala Phe Ile Gln Arg Ser His Leu Ile Gly His His Arg Val
275 280 285
His Thr Gly Val Lys Pro Tyr Lys Cys Lys Glu Cys Gly Lys Asp
290 295 300
Phe Ser Gly Arg Thr Gly Leu Ile Gln His Gln Arg Ile His Thr
305 310 315
Gly Glu Lys Pro Tyr Glu Cys Asp Glu Cys Gly Arg Pro Phe Arg
320 325 330
Val Ser Ser Ala Leu Ile Arg His Gln Arg Ile His Thr Ala Asn
335 340 345
Lys Leu Tyr

<210> 8
<211> 181
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 494740CD1

<400> 8

```
Met Glu Glu Ile Pro Ala Gln Glu Ala Ala Gly Ser Pro Arg Val
 1               5                  10                  15
Gln Phe Gln Ser Leu Glu Thr Gln Ser Glu Cys Leu Ser Pro Glu
                20                  25                  30
Pro Gln Phe Val Gln Asp Thr Asp Met Glu Gln Gly Leu Thr Gly
                35                  40                  45
Ala Pro Pro Val Pro Gln Val Pro Ala Leu Pro Arg Glu Ala Ser
                50                  55                  60
Pro Gly Asp Gln Ala Ala Ala Leu Leu Thr Ala Arg Tyr Gln Glu
                65                  70                  75
Phe Val Thr Phe Glu Asp Val Ala Val His Leu Thr Arg Glu Glu
                80                  85                  90
Trp Gly Tyr Leu Asp Pro Val Gln Arg Asp Leu Tyr Arg Glu Val
                95                  100                 105
Met Leu Glu Asn Tyr Gly Asn Val Val Ser Leu Gly Ile Leu Leu
                110                 115                 120
Arg Leu Pro Thr Thr Arg Ile His Ser Val Asn Ser Cys Pro Ala
                125                 130                 135
Leu Ser His Thr Gln Ala Ser Ala Phe Ser Gly Glu Thr Leu Ala
                140                 145                 150
Val Leu Thr Ala Gly Ile Ser Lys Arg Trp Pro Lys Tyr Arg Leu
                155                 160                 165
Pro Ile Asp Ile Ala Arg Pro Cys Ser Glu Thr Pro Phe Pro Arg
                170                 175                 180
Leu
```

<210> 9
<211> 126
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 507475CD1

<400> 9

```
Met Ser Val Met Asp Leu Ala Asn Thr Cys Ser Ser Phe Gln Ser
 1               5                  10                  15
Asp Leu Asp Phe Cys Ser Asp Cys Gly Ser Val Leu Pro Leu Pro
                20                  25                  30
Gly Ala Gln Asp Thr Val Thr Cys Ile Arg Cys Gly Phe Asn Ile
                35                  40                  45
Asn Val Arg Asp Phe Glu Gly Lys Val Val Lys Thr Ser Val Val
                50                  55                  60
Phe His Gln Leu Gly Thr Ala Met Pro Met Ser Val Glu Glu Gly
                65                  70                  75
Pro Glu Cys Gln Gly Pro Val Val Asp Arg Arg Cys Pro Arg Cys
                80                  85                  90
Gly His Glu Gly Met Ala Tyr His Thr Arg Gln Met Arg Ser Ala
                95                  100                 105
Asp Glu Gly Gln Thr Val Phe Tyr Thr Cys Thr Asn Cys Lys Phe
                110                 115                 120
Gln Glu Lys Glu Asp Ser
                125
```

<210> 10
<211> 610
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature

<223> Incyte ID No: 531581CD1

<400> 10

```
Met Gln Tyr Ser His His Cys Glu His Leu Leu Glu Arg Leu Asn
 1               5                  10                  15
Lys Gln Arg Glu Ala Gly Phe Leu Cys Asp Cys Thr Ile Val Ile
                20                  25                  30
Gly Glu Phe Gln Phe Lys Ala His Arg Asn Val Leu Ala Ser Phe
                35                  40                  45
Ser Glu Tyr Phe Gly Ala Ile Tyr Arg Ser Thr Ser Glu Asn Asn
                50                  55                  60
Val Phe Leu Asp Gln Ser Gln Val Lys Ala Asp Gly Phe Gln Lys
                65                  70                  75
Leu Leu Glu Phe Ile Tyr Thr Gly Thr Leu Asn Leu Asp Ser Trp
                80                  85                  90
Asn Val Lys Glu Ile His Gln Ala Ala Asp Tyr Leu Lys Val Glu
                95                 100                 105
Glu Val Val Thr Lys Cys Lys Ile Lys Met Glu Asp Phe Ala Phe
               110                 115                 120
Ile Ala Asn Pro Ser Ser Thr Glu Ile Ser Ser Ile Thr Gly Asn
               125                 130                 135
Ile Glu Leu Asn Gln Gln Thr Cys Leu Leu Thr Leu Arg Asp Tyr
               140                 145                 150
Asn Asn Arg Glu Lys Ser Glu Val Ser Thr Asp Leu Ile Gln Ala
               155                 160                 165
Asn Pro Lys Gln Gly Ala Leu Ala Lys Lys Ser Ser Gln Thr Lys
               170                 175                 180
Lys Lys Lys Lys Ala Phe Asn Ser Pro Lys Thr Gly Gln Asn Lys
               185                 190                 195
Thr Val Gln Tyr Pro Ser Asp Ile Leu Glu Asn Ala Ser Val Glu
               200                 205                 210
Leu Phe Leu Asp Ala Asn Lys Leu Pro Thr Pro Val Val Glu Gln
               215                 220                 225
Val Ala Gln Ile Asn Asp Asn Ser Glu Leu Glu Leu Thr Ser Val
               230                 235                 240
Val Glu Asn Thr Phe Pro Ala Gln Asp Ile Val His Thr Val Thr
               245                 250                 255
Val Lys Arg Lys Arg Gly Lys Ser Gln Pro Asn Cys Ala Leu Lys
               260                 265                 270
Glu His Ser Met Ser Asn Ile Ala Ser Val Lys Ser Pro Tyr Glu
               275                 280                 285
Ala Glu Asn Ser Gly Glu Glu Leu Asp Gln Arg Tyr Ser Lys Ala
               290                 295                 300
Lys Pro Met Cys Asn Thr Cys Gly Lys Val Phe Ser Glu Ala Ser
               305                 310                 315
Ser Leu Arg Arg His Met Arg Ile His Lys Gly Val Lys Pro Tyr
               320                 325                 330
Val Cys His Leu Cys Gly Lys Ala Phe Thr Gln Cys Asn Gln Leu
               335                 340                 345
Lys Thr His Val Arg Thr His Thr Gly Glu Lys Pro Tyr Lys Cys
               350                 355                 360
Glu Leu Cys Asp Lys Gly Phe Ala Gln Lys Cys Gln Leu Val Phe
               365                 370                 375
His Ser Arg Met His His Gly Glu Glu Lys Pro Tyr Lys Cys Asp
               380                 385                 390
Val Cys Asn Leu Gln Phe Ala Thr Ser Ser Asn Leu Lys Ile His
               395                 400                 405
Ala Arg Lys His Ser Gly Glu Lys Pro Tyr Val Cys Asp Arg Cys
               410                 415                 420
Gly Gln Arg Phe Ala Gln Ala Ser Thr Leu Thr Tyr His Val Arg
               425                 430                 435
Arg His Thr Gly Glu Lys Pro Tyr Val Cys Asp Thr Cys Gly Lys
               440                 445                 450
```

Ala Phe Ala Val Ser Ser Ser Leu Ile Thr His Ser Arg Lys His
455 460 465
Thr Gly Glu Lys Pro Tyr Ile Cys Gly Ile Cys Gly Lys Ser Phe
470 475 480
Ile Ser Ser Gly Glu Leu Asn Lys His Phe Arg Ser His Thr Gly
485 490 495
Glu Arg Pro Phe Ile Cys Glu Leu Cys Gly Asn Ser Tyr Thr Asp
500 505 510
Ile Lys Asn Leu Lys Lys His Lys Thr Lys Val His Ser Gly Ala
515 520 525
Asp Lys Thr Leu Asp Ser Ser Ala Glu Asp His Thr Leu Ser Glu
530 535 540
Gln Asp Ser Ile Gln Lys Ser Pro Leu Ser Glu Thr Met Asp Val
545 550 555
Lys Pro Ser Asp Met Thr Leu Pro Leu Ala Leu Pro Leu Gly Thr
560 565 570
Glu Asp His His Met Leu Leu Pro Val Thr Asp Thr Gln Ser Pro
575 580 585
Thr Ser Asp Thr Leu Leu Arg Ser Thr Val Asn Gly Tyr Ser Glu
590 595 600
Pro Gln Leu Ile Phe Leu Gln Gln Leu Tyr
605 610

<210> 11
<211> 111
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 675190CD1

<400> 11
Met Lys Asn Ala Thr Ile Val Met Ser Val Arg Arg Glu Gln Gly
1 5 10 15
Ser Ser Ser Gly Glu Gly Ser Leu Ser Phe Glu Asp Val Ala Val
20 25 30
Gly Phe Thr Arg Glu Glu Trp Gln Phe Leu Asp Gln Ser Gln Lys
35 40 45
Val Leu Tyr Lys Glu Val Met Leu Glu Asn Tyr Ile Asn Leu Val
50 55 60
Ser Ile Gly Tyr Arg Gly Thr Lys Pro Asp Ser Leu Phe Lys Leu
65 70 75
Glu Gln Gly Glu Pro Pro Gly Ile Ala Glu Gly Ala Ala His Ser
80 85 90
Gln Ile Cys Pro Gly Tyr Ser Phe Arg Arg Arg Thr Leu Gln Met
95 100 105
Glu Gly Met Gln Glu Ser
110

<210> 12
<211> 152
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 685434CD1

<400> 12
Met Leu Tyr Leu Ala Thr Arg Ile Glu Gln Glu Asn Val Ile Asn
1 5 10 15
His Thr Asp Glu Glu Gly Phe Thr Pro Leu Met Trp Ala Ala Ala

```
                 20                       25                       30
His Gly Gln Ile Ala Val Val Glu Phe Leu Leu Gln Asn Gly Ala
                 35                       40                       45
Asp Pro Gln Leu Leu Gly Lys Gly Arg Glu Ser Ala Leu Ser Leu
                 50                       55                       60
Ala Cys Ser Lys Gly Tyr Thr Asp Ile Val Lys Met Leu Leu Asp
                 65                       70                       75
Cys Gly Val Asp Val Asn Glu Tyr Asp Trp Asn Gly Gly Thr Pro
                 80                       85                       90
Leu Leu Tyr Ala Val His Gly Asn His Val Lys Cys Val Lys Met
                 95                      100                      105
Leu Leu Glu Ser Gly Ala Asp Pro Thr Ile Glu Thr Asp Ser Gly
                110                      115                      120
Tyr Asn Ser Met Asp Leu Ala Val Ala Leu Gly Tyr Arg Ser Val
                125                      130                      135
Gln Gln Val Ile Glu Ser His Leu Leu Lys Leu Leu Gln Asn Ile
                140                      145                      150
Lys Glu
```

<210> 13
<211> 131
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 788663CD1

<400> 13

```
Met Ala Asp Val Val Val Gly Lys Asp Lys Gly Gly Glu Gln Arg
  1               5                       10                       15
Leu Ile Ser Leu Pro Leu Ser Arg Ile Arg Val Ile Met Lys Ser
                 20                       25                       30
Ser Pro Glu Val Ser Ser Ile Asn Gln Glu Ala Leu Val Leu Thr
                 35                       40                       45
Ala Lys Ala Thr Glu Leu Phe Val Gln Cys Leu Ala Thr Tyr Ser
                 50                       55                       60
Tyr Arg His Gly Ser Gly Lys Glu Lys Lys Val Leu Thr Tyr Ser
                 65                       70                       75
Asp Leu Ala Asn Thr Ala Gln Gln Ser Glu Thr Phe Gln Phe Leu
                 80                       85                       90
Ala Asp Ile Leu Pro Lys Lys Ile Leu Ala Ser Lys Tyr Leu Lys
                 95                      100                      105
Met Leu Lys Glu Glu Lys Arg Glu Glu Asp Glu Glu Asn Asp Asn
                110                      115                      120
Asp Asn Glu Ser Asp His Asp Glu Ala Asp Ser
                125                      130
```

<210> 14
<211> 541
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 870100CD1

<400> 14

```
Met Pro Arg Arg Lys Gln Ser His Pro Gln Pro Val Lys Cys Glu
  1               5                       10                       15
Gly Val Lys Val Asp Thr Glu Asp Ser Leu Asp Glu Gly Pro Gly
                 20                       25                       30
```

Ala Leu Val Leu Glu Ser Asp Leu Leu Leu Gly Gln Asp Leu Glu
35 40 45
Phe Glu Glu Glu Glu Glu Glu Glu Glu Gly Asp Gly Asn Ser Asp
50 55 60
Gln Leu Met Gly Phe Glu Arg Asp Ser Glu Gly Asp Ser Leu Gly
65 70 75
Ala Arg Pro Gly Leu Pro Tyr Gly Leu Ser Asp Asp Glu Ser Gly
80 85 90
Gly Gly Arg Ala Leu Ser Ala Glu Ser Glu Val Glu Glu Pro Ala
95 100 105
Arg Gly Pro Gly Glu Ala Arg Gly Glu Arg Pro Gly Pro Ala Cys
110 115 120
Gln Leu Cys Gly Gly Pro Thr Gly Glu Gly Pro Cys Cys Gly Ala
125 130 135
Gly Gly Pro Gly Gly Gly Pro Leu Leu Pro Pro Arg Leu Leu Tyr
140 145 150
Ser Cys Arg Leu Cys Thr Phe Val Ser His Tyr Ser Ser His Leu
155 160 165
Lys Arg His Met Gln Thr His Ser Gly Glu Lys Pro Phe Arg Cys
170 175 180
Gly Arg Cys Pro Tyr Ala Ser Ala Gln Leu Val Asn Leu Thr Arg
185 190 195
His Thr Arg Thr His Thr Gly Glu Lys Pro Tyr Arg Cys Pro His
200 205 210
Cys Pro Phe Ala Cys Ser Ser Leu Gly Asn Leu Arg Arg His Gln
215 220 225
Arg Thr His Ala Gly Pro Pro Thr Pro Pro Cys Pro Thr Cys Gly
230 235 240
Phe Arg Cys Cys Thr Pro Arg Pro Ala Arg Pro Pro Ser Pro Thr
245 250 255
Glu Gln Glu Gly Ala Val Pro Arg Arg Pro Glu Asp Ala Leu Leu
260 265 270
Leu Pro Asp Leu Ser Leu His Val Pro Pro Gly Gly Ala Ser Phe
275 280 285
Leu Pro Asp Cys Gly Gln Leu Arg Gly Glu Gly Glu Gly Leu Cys
290 295 300
Gly Thr Gly Ser Glu Pro Leu Pro Glu Leu Leu Phe Pro Trp Thr
305 310 315
Cys Arg Gly Cys Gly Gln Glu Leu Glu Glu Gly Glu Gly Ser Arg
320 325 330
Leu Gly Ala Ala Met Cys Gly Arg Cys Met Arg Gly Glu Ala Gly
335 340 345
Gly Gly Ala Ser Gly Gly Pro Gln Gly Pro Ser Asp Lys Gly Phe
350 355 360
Ala Cys Ser Leu Cys Pro Phe Ala Thr His Tyr Pro Asn His Leu
365 370 375
Ala Arg His Met Lys Thr His Ser Gly Glu Lys Pro Phe Arg Cys
380 385 390
Ala Arg Cys Pro Tyr Ala Ser Ala His Leu Asp Asn Leu Lys Arg
395 400 405
His Gln Arg Val His Thr Gly Glu Lys Pro Tyr Lys Cys Pro Leu
410 415 420
Cys Pro Tyr Ala Cys Gly Asn Leu Ala Asn Leu Lys Arg His Gly
425 430 435
Arg Ile His Ser Gly Asp Lys Pro Phe Arg Cys Ser Leu Cys Asn
440 445 450
Tyr Ser Cys Asn Gln Ser Met Asn Leu Lys Arg His Met Leu Arg
455 460 465
His Thr Gly Glu Lys Pro Phe Arg Cys Ala Thr Cys Ala Tyr Thr
470 475 480
Thr Gly His Trp Asp Asn Tyr Lys Arg His Gln Lys Val His Gly
485 490 495
His Gly Gly Ala Gly Gly Pro Gly Leu Ser Ala Ser Glu Gly Trp

500 505 510
Ala Pro Pro His Ser Pro Pro Ser Val Leu Ser Ser Arg Gly Pro
515 520 525
Pro Ala Leu Gly Thr Ala Gly Ser Arg Ala Val His Thr Asp Ser
530 535 540
Ser

<210> 15
<211> 1828
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 879500CD1

<400> 15
Met Pro Thr Pro Thr Leu Val Arg Pro Leu Leu Lys Leu Val His
1 5 10 15
Ser Pro Ser Pro Glu Val Ser Ala Ser Ala Pro Gly Ala Ala Pro
20 25 30
Leu Thr Ile Ser Ser Pro Leu His Val Pro Ser Ser Leu Pro Gly
35 40 45
Pro Ala Ser Ser Pro Met Pro Ile Pro Asn Ser Ser Pro Leu Ala
50 55 60
Ser Pro Val Ser Ser Thr Val Ser Val Pro Leu Ser Ser Ser Leu
65 70 75
Pro Ile Ser Val Pro Thr Thr Leu Pro Ala Pro Ala Ser Ala Pro
80 85 90
Leu Thr Ile Pro Ile Ser Ala Pro Leu Thr Val Ser Ala Ser Gly
95 100 105
Pro Ala Leu Leu Thr Ser Val Thr Pro Pro Leu Ala Pro Val Val
110 115 120
Pro Ala Ala Pro Gly Pro Pro Ser Leu Ala Pro Ser Gly Ala Ser
125 130 135
Pro Ser Ala Ser Ala Leu Thr Leu Gly Leu Ala Thr Ala Pro Ser
140 145 150
Leu Ser Ser Ser Gln Thr Pro Gly His Pro Leu Leu Leu Ala Pro
155 160 165
Thr Ser Ser His Val Pro Gly Leu Asn Ser Thr Val Ala Pro Ala
170 175 180
Cys Ser Pro Val Leu Val Pro Ala Ser Ala Leu Ala Ser Pro Phe
185 190 195
Pro Ser Ala Pro Asn Pro Ala Pro Pro Leu Ala Pro Leu Pro Val
200 205 210
Leu Ala Pro Ser Pro Gly Ala Ala Pro Val Leu Ala Ser Ser Gln
215 220 225
Thr Pro Val Pro Val Met Ala Pro Ser Ser Thr Pro Gly Thr Ser
230 235 240
Leu Ala Ser Ala Ser Pro Val Pro Ala Pro Thr Pro Val Leu Ala
245 250 255
Pro Ser Ser Thr Gln Thr Met Leu Pro Ala Pro Val Pro Ser Pro
260 265 270
Leu Pro Ser Pro Ala Ser Thr Gln Thr Leu Ala Leu Ala Pro Ala
275 280 285
Leu Ala Pro Thr Leu Gly Gly Ser Ser Pro Ser Gln Thr Leu Ser
290 295 300
Leu Gly Thr Gly Asn Pro Gln Gly Pro Phe Pro Thr Gln Thr Leu
305 310 315
Ser Leu Thr Pro Ala Ser Ser Leu Val Pro Thr Pro Ala Gln Thr
320 325 330
Leu Ser Leu Ala Pro Gly Pro Pro Leu Gly Pro Thr Gln Thr Leu

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                335                      340                      345
Ser Leu Ala Pro Ala Pro Pro Leu Ala Pro Ala Ser Pro Val Gly
                350                      355                      360
Pro Ala Pro Ala His Thr Leu Thr Leu Ala Pro Ala Ser Ser Ser
                365                      370                      375
Ala Ser Leu Leu Ala Pro Ala Ser Val Gln Thr Leu Thr Leu Ser
                380                      385                      390
Pro Ala Pro Val Pro Thr Leu Gly Pro Ala Ala Ala Gln Thr Leu
                395                      400                      405
Ala Leu Ala Pro Ala Ser Thr Gln Ser Pro Ala Ser Gln Ala Ser
                410                      415                      420
Ser Leu Val Val Ser Ala Ser Gly Ala Ala Pro Leu Pro Val Thr
                425                      430                      435
Met Val Ser Arg Leu Pro Val Ser Lys Asp Glu Pro Asp Thr Leu
                440                      445                      450
Thr Leu Arg Ser Gly Pro Pro Ser Pro Pro Ser Thr Ala Thr Ser
                455                      460                      465
Phe Gly Gly Pro Arg Pro Arg Arg Gln Pro Pro Pro Pro Pro Arg
                470                      475                      480
Ser Pro Phe Tyr Leu Asp Ser Leu Glu Glu Lys Arg Lys Arg Gln
                485                      490                      495
Arg Ser Glu Arg Leu Glu Arg Ile Phe Gln Leu Ser Glu Ala His
                500                      505                      510
Gly Ala Leu Ala Pro Val Tyr Gly Thr Glu Val Leu Asp Phe Cys
                515                      520                      525
Thr Leu Pro Gln Pro Val Ala Ser Pro Ile Gly Pro Arg Ser Pro
                530                      535                      540
Gly Pro Ser His Pro Thr Phe Trp Thr Tyr Thr Glu Ala Ala His
                545                      550                      555
Arg Ala Val Leu Phe Pro Gln Gln Arg Leu Asp Gln Leu Ser Glu
                560                      565                      570
Ile Ile Glu Arg Phe Ile Phe Val Met Pro Pro Val Glu Ala Pro
                575                      580                      585
Pro Pro Ser Leu His Ala Cys His Pro Pro Pro Trp Leu Ala Pro
                590                      595                      600
Arg Gln Ala Ala Phe Gln Glu Gln Leu Ala Ser Glu Leu Trp Pro
                605                      610                      615
Arg Ala Arg Pro Leu His Arg Ile Val Cys Asn Met Arg Thr Gln
                620                      625                      630
Phe Pro Asp Leu Arg Leu Ile Gln Tyr Asp Cys Gly Lys Leu Gln
                635                      640                      645
Thr Leu Ala Val Leu Leu Arg Gln Leu Lys Ala Glu Gly His Arg
                650                      655                      660
Val Leu Ile Phe Thr Gln Met Thr Arg Met Leu Asp Val Leu Glu
                665                      670                      675
Gln Phe Leu Thr Tyr His Gly His Leu Tyr Leu Arg Leu Asp Gly
                680                      685                      690
Ser Thr Arg Val Glu Gln Arg Gln Ala Leu Met Glu Arg Phe Asn
                695                      700                      705
Ala Asp Lys Arg Ile Phe Cys Phe Ile Leu Ser Thr Arg Ser Gly
                710                      715                      720
Gly Val Gly Val Asn Leu Thr Gly Ala Asp Thr Val Val Phe Tyr
                725                      730                      735
Asp Ser Asp Trp Asn Pro Thr Met Asp Ala Gln Ala Gln Asp Arg
                740                      745                      750
Cys His Arg Ile Gly Gln Thr Arg Asp Val His Ile Tyr Arg Leu
                755                      760                      765
Ile Ser Glu Arg Thr Val Glu Glu Asn Ile Leu Lys Lys Ala Asn
                770                      775                      780
Gln Lys Arg Met Leu Gly Asp Met Ala Ile Glu Gly Gly Asn Phe
                785                      790                      795
Thr Thr Ala Tyr Phe Lys Gln Thr Ile Arg Glu Leu Phe Asp Met
                800                      805                      810
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Pro Leu Glu Glu Pro Ser Ser Ser Ser Val Pro Ser Ala Pro Glu
815 820 825
Glu Glu Glu Glu Thr Val Ala Ser Lys Gln Thr His Ile Leu Glu
830 835 840
Gln Ala Leu Cys Arg Ala Glu Asp Glu Glu Asp Ile Arg Ala Ala
845 850 855
Thr Gln Ala Lys Ala Glu Gln Val Ala Glu Leu Ala Glu Phe Asn
860 865 870
Glu Asn Asp Gly Phe Pro Ala Gly Glu Gly Glu Glu Ala Gly Arg
875 880 885
Pro Gly Ala Glu Asp Glu Glu Met Ser Arg Ala Glu Gln Glu Ile
890 895 900
Ala Ala Leu Val Glu Gln Leu Thr Pro Ile Glu Arg Tyr Ala Met
905 910 915
Lys Phe Leu Glu Ala Ser Leu Glu Glu Val Ser Arg Glu Glu Leu
920 925 930
Lys Gln Ala Glu Glu Gln Val Glu Ala Ala Arg Lys Asp Leu Asp
935 940 945
Gln Ala Lys Glu Glu Val Phe Arg Leu Pro Gln Glu Glu Glu Glu
950 955 960
Gly Pro Gly Ala Gly Asp Glu Ser Ser Cys Gly Thr Gly Gly Gly
965 970 975
Thr His Arg Arg Ser Lys Lys Ala Lys Ala Pro Glu Arg Pro Gly
980 985 990
Thr Arg Val Ser Glu Arg Leu Arg Gly Ala Arg Ala Glu Thr Gln
995 1000 1005
Gly Ala Asn His Thr Pro Val Ile Ser Ala His Gln Thr Arg Ser
1010 1015 1020
Thr Thr Thr Pro Pro Arg Cys Ser Pro Ala Arg Glu Arg Val Pro
1025 1030 1035
Arg Pro Ala Pro Arg Pro Arg Pro Thr Pro Ala Ser Ala Pro Ala
1040 1045 1050
Ala Ile Pro Ala Leu Val Pro Val Pro Val Ser Ala Pro Val Pro
1055 1060 1065
Ile Ser Ala Pro Asn Pro Ile Thr Ile Leu Pro Val His Ile Leu
1070 1075 1080
Pro Ser Pro Pro Pro Pro Ser Gln Ile Pro Pro Cys Ser Ser Pro
1085 1090 1095
Ala Cys Thr Pro Pro Pro Ala Cys Thr Pro Pro Pro Ala His Thr
1100 1105 1110
Pro Pro Pro Ala Gln Thr Cys Leu Val Thr Pro Ser Ser Pro Leu
1115 1120 1125
Leu Leu Gly Pro Pro Ser Val Pro Ile Ser Ala Ser Val Thr Asn
1130 1135 1140
Leu Pro Leu Gly Leu Arg Pro Glu Ala Glu Leu Cys Ala Gln Ala
1145 1150 1155
Leu Ala Ser Pro Glu Ser Leu Glu Leu Ala Ser Val Ala Ser Ser
1160 1165 1170
Glu Thr Ser Ser Leu Ser Leu Val Pro Pro Lys Asp Leu Leu Pro
1175 1180 1185
Val Ala Val Glu Ile Leu Pro Val Ser Glu Lys Asn Leu Ser Leu
1190 1195 1200
Thr Pro Ser Ala Pro Ser Leu Thr Leu Glu Ala Gly Ser Ile Pro
1205 1210 1215
Asn Gly Gln Glu Gln Glu Ala Pro Asp Ser Ala Glu Gly Thr Thr
1220 1225 1230
Leu Thr Val Leu Pro Glu Gly Glu Glu Leu Pro Leu Cys Val Ser
1235 1240 1245
Glu Ser Asn Gly Leu Glu Leu Pro Pro Ser Ala Ala Ser Asp Glu
1250 1255 1260
Pro Leu Gln Glu Pro Leu Glu Ala Asp Arg Thr Ser Glu Glu Leu
1265 1270 1275
Thr Glu Ala Lys Thr Pro Thr Ser Ser Pro Glu Lys Pro Gln Glu

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                1280                        1285                        1290
Leu Val Thr Ala Glu Val Ala Ala Pro Ser Thr Ser Ser Ser Ala
                1295                        1300                        1305
Thr Ser Ser Pro Glu Gly Pro Ser Pro Ala Arg Pro Pro Arg Arg
                1310                        1315                        1320
Arg Thr Ser Ala Asp Val Glu Ile Arg Gly Gln Gly Thr Gly Arg
                1325                        1330                        1335
Pro Gly Gln Pro Pro Gly Pro Lys Val Leu Arg Lys Leu Pro Gly
                1340                        1345                        1350
Arg Leu Val Thr Val Val Glu Glu Lys Glu Leu Val Arg Arg Arg
                1355                        1360                        1365
Arg Gln Gln Arg Gly Ala Ala Ser Thr Leu Val Pro Gly Val Ser
                1370                        1375                        1380
Glu Thr Ser Ala Ser Pro Gly Ser Pro Ser Val Arg Ser Met Ser
                1385                        1390                        1395
Gly Pro Glu Ser Ser Pro Pro Ile Gly Gly Pro Cys Glu Ala Ala
                1400                        1405                        1410
Pro Ser Ser Ser Leu Pro Thr Pro Pro Gln Gln Pro Phe Ile Ala
                1415                        1420                        1425
Arg Arg His Ile Glu Leu Gly Val Thr Gly Gly Gly Ser Pro Glu
                1430                        1435                        1440
Asn Gly Asp Gly Ala Leu Leu Ala Ile Thr Pro Pro Ala Val Lys
                1445                        1450                        1455
Arg Arg Arg Gly Arg Pro Pro Lys Lys Asn Arg Ser Pro Ala Asp
                1460                        1465                        1470
Ala Gly Arg Gly Val Asp Glu Ala Pro Ser Ser Thr Leu Lys Gly
                1475                        1480                        1485
Lys Thr Asn Gly Ala Asp Pro Val Pro Gly Pro Glu Thr Leu Ile
                1490                        1495                        1500
Val Ala Asp Pro Val Leu Glu Pro Gln Leu Ile Pro Gly Pro Gln
                1505                        1510                        1515
Pro Leu Gly Pro Gln Pro Val His Arg Pro Asn Pro Leu Leu Ser
                1520                        1525                        1530
Pro Val Glu Lys Arg Arg Arg Gly Arg Pro Pro Lys Ala Arg Asp
                1535                        1540                        1545
Leu Pro Ile Pro Gly Thr Ile Ser Ser Ala Gly Asp Gly Asn Ser
                1550                        1555                        1560
Glu Ser Arg Thr Gln Pro Pro Pro His Pro Ser Pro Leu Thr Pro
                1565                        1570                        1575
Leu Pro Pro Leu Leu Val Cys Pro Thr Ala Thr Val Ala Asn Thr
                1580                        1585                        1590
Val Thr Thr Val Thr Ile Ser Thr Ser Pro Pro Lys Arg Lys Arg
                1595                        1600                        1605
Gly Arg Pro Pro Lys Asn Pro Pro Ser Pro Arg Pro Ser Gln Leu
                1610                        1615                        1620
Pro Val Leu Asp Arg Asp Ser Thr Ser Val Leu Glu Ser Cys Gly
                1625                        1630                        1635
Leu Gly Arg Arg Arg Gln Pro Gln Gly Gln Gly Glu Ser Glu Gly
                1640                        1645                        1650
Ser Ser Ser Asp Glu Asp Gly Ser Arg Pro Leu Thr Arg Leu Ala
                1655                        1660                        1665
Arg Leu Arg Leu Glu Ala Glu Gly Met Arg Gly Arg Lys Ser Gly
                1670                        1675                        1680
Gly Ser Met Val Val Ala Val Ile Gln Asp Asp Leu Asp Leu Ala
                1685                        1690                        1695
Asp Ser Gly Pro Gly Gly Leu Glu Leu Thr Pro Pro Val Val Ser
                1700                        1705                        1710
Leu Thr Pro Lys Leu Arg Ser Thr Arg Leu Arg Pro Gly Ser Leu
                1715                        1720                        1725
Val Pro Pro Leu Glu Thr Glu Lys Leu Pro Arg Lys Arg Ala Gly
                1730                        1735                        1740
Ala Pro Val Gly Gly Ser Pro Gly Leu Ala Lys Arg Gly Arg Leu
                1745                        1750                        1755
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Gln Pro Pro Ser Pro Leu Gly Pro Glu Gly Ser Val Glu Glu Ser
                1760                1765                1770
Glu Ala Glu Ala Ser Gly Glu Glu Glu Glu Gly Asp Gly Thr Pro
                1775                1780                1785
Arg Arg Arg Pro Gly Pro Arg Arg Leu Val Gly Thr Thr Asn Gln
                1790                1795                1800
Gly Asp Gln Arg Ile Leu Arg Ser Ser Ala Pro Pro Ser Leu Ala
                1805                1810                1815
Gly Pro Ala Val Ser His Arg Gly Arg Lys Ala Lys Thr
                1820                1825

<210> 16
<211> 482
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 975377CD1

<400> 16
Met Ala Glu Ala Ala Thr Pro Gly Thr Thr Ala Thr Thr Ser Gly
 1               5                  10                  15
Ala Gly Ala Ala Ala Ala Thr Ala Ala Ala Ala Ser Pro Thr Pro
                20                  25                  30
Ile Pro Thr Val Thr Ala Pro Ser Leu Gly Ala Gly Gly Gly Gly
                35                  40                  45
Gly Gly Ser Asp Gly Ser Gly Gly Gly Trp Thr Lys Gln Val Thr
                50                  55                  60
Cys Arg Tyr Phe Met His Gly Val Cys Lys Glu Gly Asp Asn Cys
                65                  70                  75
Arg Tyr Ser His Asp Leu Ser Asp Ser Pro Tyr Ser Val Val Cys
                80                  85                  90
Lys Tyr Phe Gln Arg Gly Tyr Cys Ile Tyr Gly Asp Arg Cys Arg
                95                  100                 105
Tyr Glu His Ser Lys Pro Leu Lys Gln Glu Glu Ala Thr Ala Thr
                110                 115                 120
Glu Leu Thr Thr Lys Ser Ser Leu Ala Ala Ser Ser Ser Leu Ser
                125                 130                 135
Ser Ile Val Gly Pro Leu Val Glu Met Asn Thr Gly Glu Ala Glu
                140                 145                 150
Ser Arg Asn Ser Asn Phe Ala Thr Val Gly Ala Gly Ser Glu Asp
                155                 160                 165
Trp Val Asn Ala Ile Glu Phe Val Pro Gly Gln Pro Tyr Cys Gly
                170                 175                 180
Arg Thr Ala Pro Ser Cys Thr Glu Ala Pro Leu Gln Gly Ser Val
                185                 190                 195
Thr Lys Glu Glu Ser Glu Lys Glu Gln Thr Ala Val Glu Thr Lys
                200                 205                 210
Lys Gln Leu Cys Pro Tyr Ala Ala Val Gly Glu Cys Arg Tyr Gly
                215                 220                 225
Glu Asn Cys Val Tyr Leu His Gly Asp Ser Cys Asp Met Cys Gly
                230                 235                 240
Leu Gln Val Leu His Pro Met Asp Ala Ala Gln Arg Ser Gln His
                245                 250                 255
Ile Lys Ser Cys Ile Glu Ala His Glu Lys Asp Met Glu Leu Ser
                260                 265                 270
Phe Ala Val Gln Arg Ser Lys Asp Met Val Cys Gly Ile Cys Met
                275                 280                 285
Glu Val Val Tyr Glu Lys Ala Asn Pro Ser Glu Arg Arg Phe Gly
                290                 295                 300
Ile Leu Ser Asn Cys Asn His Thr Tyr Cys Leu Lys Cys Ile Arg
                305                 310                 315
```

Lys Trp Arg Ser Ala Lys Gln Phe Glu Ser Lys Ile Ile Lys Ser
320 325 330
Cys Pro Glu Cys Arg Ile Thr Ser Asn Phe Val Ile Pro Ser Glu
335 340 345
Tyr Trp Val Glu Glu Lys Glu Glu Lys Gln Lys Leu Ile Leu Lys
350 355 360
Tyr Lys Glu Ala Met Ser Asn Lys Ala Cys Arg Tyr Phe Asp Glu
365 370 375
Gly Arg Gly Ser Cys Pro Phe Gly Gly Asn Cys Phe Tyr Lys His
380 385 390
Ala Tyr Pro Asp Gly Arg Arg Glu Glu Pro Gln Arg Gln Lys Val
395 400 405
Gly Thr Ser Ser Arg Tyr Arg Ala Gln Arg Arg Asn His Phe Trp
410 415 420
Glu Leu Ile Glu Glu Arg Glu Asn Ser Asn Pro Phe Asp Asn Asp
425 430 435
Glu Glu Glu Val Val Thr Phe Glu Leu Gly Glu Met Leu Leu Met
440 445 450
Leu Leu Ala Ala Gly Gly Asp Asp Glu Leu Thr Asp Ser Glu Asp
455 460 465
Glu Trp Asp Leu Phe His Asp Glu Leu Glu Asp Phe Tyr Asp Leu
470 475 480
Asp Leu

<210> 17
<211> 264
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1208721CD1

<400> 17
Met Leu Gly Ile Leu Ile Tyr Ile Gln Asn Ser Asp Tyr Glu Glu
1 5 10 15
Ile Thr Ile Asp Pro Thr Cys Ser Trp Lys Pro Val Pro Val Lys
20 25 30
Pro Asp Met His Ile Lys Glu Glu Pro Asp Gly Pro Ala Leu Lys
35 40 45
Arg Cys Arg Thr Val Ser Pro Ala His Val Leu Met Pro Ser Val
50 55 60
Met Glu Met Ile Ala Ala Leu Gly Pro Gly Ala Ala Pro Phe Ala
65 70 75
Pro Leu Gln Pro Pro Ser Val Pro Ala Pro Ser Asp Tyr Pro Gly
80 85 90
Gln Gly Ser Ser Phe Leu Gly Pro Gly Thr Phe Pro Glu Ser Phe
95 100 105
Pro Pro Thr Thr Pro Ser Thr Pro Thr Leu Ala Glu Phe Thr Pro
110 115 120
Gly Pro Pro Pro Ile Ser Tyr Gln Ser Asp Ile Pro Ser Ser Leu
125 130 135
Leu Thr Ser Glu Lys Ser Thr Ala Cys Leu Pro Ser Gln Met Ala
140 145 150
Pro Ala Gly His Leu Asp Pro Thr His Asn Pro Gly Thr Pro Gly
155 160 165
Leu His Thr Ser Asn Leu Gly Ala Pro Pro Gly Pro Gln Leu His
170 175 180
His Ser Asn Pro Pro Pro Ala Ser Arg Gln Ser Leu Gly Gln Ala
185 190 195
Ser Leu Gly Pro Thr Gly Glu Leu Ala Phe Ser Pro Ala Thr Gly
200 205 210

```
Val Met Gly Pro Pro Ser Met Ser Gly Ala Gly Glu Ala Pro Glu
                215                 220                 225
Pro Ala Leu Asp Leu Leu Pro Glu Leu Thr Asn Pro Asp Glu Leu
                230                 235                 240
Leu Ser Tyr Leu Gly Pro Pro Asp Leu Pro Thr Asn Asn Asn Asp
                245                 250                 255
Asp Leu Leu Ser Leu Phe Glu Asn Asn
                260

<210> 18
<211> 350
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1234329CD1

<400> 18
Met Pro Pro Pro Tyr Ala Ser Leu Thr Arg Pro Leu His His Gln
 1               5                  10                  15
Ala Ser Ala Cys Pro His Ser His Gly Asn Pro Pro Pro Gln Thr
                20                  25                  30
Gln Pro Pro Pro Gln Val Asp Tyr Val Ile Pro His Pro Val His
                35                  40                  45
Ala Phe His Ser Gln Ile Ser Ser His Ala Thr Ser His Pro Val
                50                  55                  60
Ala Pro Pro Pro Pro Thr His Leu Ala Ser Thr Ala Ala Pro Ile
                65                  70                  75
Pro Gln His Leu Pro Pro Thr His Gln Pro Ile Ser His His Ile
                80                  85                  90
Pro Ala Thr Ala Pro Pro Ala Gln Arg Leu His Pro His Glu Val
                95                 100                 105
Met Gln Arg Met Glu Val Gln Arg Arg Arg Met Met Gln His Pro
               110                 115                 120
Thr Gly Leu Phe Val Phe Cys Val Ser Arg Arg Ala His Glu Arg
               125                 130                 135
Pro Pro Pro His Pro His Arg Met His Pro Asn Tyr Gly His Gly
               140                 145                 150
His His Ile His Val Pro Gln Thr Met Ser Ser His Pro Arg Gln
               155                 160                 165
Ala Pro Glu Arg Ser Ala Trp Glu Leu Gly Ile Glu Ala Gly Val
               170                 175                 180
Thr Ala Ala Thr Tyr Thr Pro Gly Ala Leu His Pro His Leu Ala
               185                 190                 195
His Tyr His Ala Pro Pro Arg Leu His His Leu Gln Leu Gly Ala
               200                 205                 210
Leu Pro Leu Met Val Pro Asp Met Ala Gly Tyr Pro His Ile Arg
               215                 220                 225
Tyr Ile Ser Ser Gly Leu Asp Gly Thr Ser Phe Arg Gly Pro Phe
               230                 235                 240
Arg Gly Asn Phe Glu Glu Leu Ile His Leu Glu Glu Arg Leu Gly
               245                 250                 255
Asn Val Asn Arg Gly Ala Ser Gln Gly Thr Ile Glu Arg Cys Thr
               260                 265                 270
Tyr Pro His Lys Tyr Lys Lys Arg Lys Leu His Cys Lys Gln Asp
               275                 280                 285
Gly Glu Glu Gly Thr Glu Glu Asp Thr Glu Glu Lys Cys Thr Ile
               290                 295                 300
Cys Leu Ser Ile Leu Glu Glu Gly Glu Asp Val Arg Arg Leu Pro
               305                 310                 315
Cys Met His Leu Phe His Gln Val Cys Val Asp Gln Trp Leu Ile
               320                 325                 330
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Thr Asn Lys Lys Cys Pro Ile Cys Arg Val Asp Ile Glu Ala Gln
                335                 340                 345
Leu Pro Ser Glu Ser
                350

&lt;210&gt; 19
&lt;211&gt; 549
&lt;212&gt; PRT
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; misc_feature
&lt;223&gt; Incyte ID No: 1238747CD1

&lt;400&gt; 19
Met Phe Thr Met Thr Arg Ala Met Glu Glu Ala Leu Phe Gln His
  1               5                  10                  15
Phe Met His Gln Lys Leu Gly Ile Ala Tyr Ala Ile His Lys Pro
                 20                  25                  30
Phe Pro Phe Phe Glu Gly Leu Leu Asp Asn Ser Ile Ile Thr Lys
                 35                  40                  45
Arg Met Tyr Met Glu Ser Leu Glu Ala Cys Arg Asn Leu Ile Pro
                 50                  55                  60
Val Ser Arg Val Val His Asn Ile Leu Thr Gln Leu Glu Arg Thr
                 65                  70                  75
Phe Asn Leu Ser Leu Leu Val Thr Leu Phe Ser Gln Ile Asn Leu
                 80                  85                  90
Arg Glu Tyr Pro Asn Leu Val Thr Ile Tyr Arg Ser Phe Lys Arg
                 95                 100                 105
Val Gly Ala Ser Tyr Glu Arg Gln Ser Arg Asp Thr Pro Ile Leu
                110                 115                 120
Leu Glu Ala Pro Thr Gly Leu Ala Glu Gly Ser Ser Leu His Thr
                125                 130                 135
Pro Leu Ala Leu Pro Pro Pro Gln Pro Pro Gln Pro Ser Cys Ser
                140                 145                 150
Pro Cys Ala Pro Arg Val Ser Glu Pro Gly Thr Ser Ser Gln Gln
                155                 160                 165
Ser Asp Glu Ile Leu Ser Glu Ser Pro Ser Pro Ser Asp Pro Val
                170                 175                 180
Leu Pro Leu Pro Ala Leu Ile Gln Glu Gly Arg Ser Thr Ser Val
                185                 190                 195
Thr Asn Asp Lys Leu Thr Ser Lys Met Asn Ala Glu Glu Asp Ser
                200                 205                 210
Glu Glu Met Pro Ser Leu Leu Thr Ser Thr Val Gln Val Ala Ser
                215                 220                 225
Asp Asn Leu Ile Pro Gln Ile Arg Asp Lys Glu Asp Pro Gln Glu
                230                 235                 240
Met Pro His Ser Pro Leu Gly Ser Met Pro Glu Ile Arg Asp Asn
                245                 250                 255
Ser Pro Glu Pro Asn Asp Pro Glu Glu Pro Gln Glu Val Ser Ser
                260                 265                 270
Thr Pro Ser Asp Lys Lys Gly Lys Lys Arg Lys Arg Cys Ile Trp
                275                 280                 285
Ser Thr Pro Lys Arg Arg His Lys Lys Lys Ser Leu Pro Arg Gly
                290                 295                 300
Thr Ala Ser Ser Arg His Gly Ile Gln Lys Lys Leu Lys Arg Val
                305                 310                 315
Asp Gln Val Pro Gln Lys Lys Asp Asp Ser Thr Cys Asn Ser Thr
                320                 325                 330
Val Glu Thr Arg Ala Gln Lys Ala Arg Thr Glu Cys Ala Arg Lys
                335                 340                 345
Ser Arg Ser Glu Glu Ile Ile Asp Gly Thr Ser Glu Met Asn Glu
                350                 355                 360
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Gly Lys Arg Ser Gln Lys Thr Pro Ser Thr Pro Arg Arg Val Thr
365 370 375
Gln Gly Ala Ala Ser Pro Gly His Gly Ile Gln Glu Lys Leu Gln
380 385 390
Val Val Asp Lys Val Thr Gln Arg Lys Asp Asp Ser Thr Trp Asn
395 400 405
Ser Glu Val Met Met Arg Val Gln Lys Ala Arg Thr Lys Cys Ala
410 415 420
Arg Lys Ser Arg Ser Lys Glu Lys Lys Lys Glu Lys Asp Ile Cys
425 430 435
Ser Ser Ser Lys Arg Arg Phe Gln Lys Asn Ile His Arg Arg Gly
440 445 450
Lys Pro Lys Ser Asp Thr Val Asp Phe His Cys Ser Lys Leu Pro
455 460 465
Val Thr Cys Gly Glu Ala Lys Gly Ile Leu Tyr Lys Lys Lys Met
470 475 480
Lys His Gly Ser Ser Val Lys Cys Ile Arg Asn Glu Asp Gly Thr
485 490 495
Trp Leu Thr Pro Asn Glu Phe Glu Val Glu Gly Lys Gly Arg Asn
500 505 510
Ala Lys Asn Trp Lys Arg Asn Ile Arg Cys Glu Gly Met Thr Leu
515 520 525
Gly Glu Leu Leu Lys Ser Gly Leu Leu Leu Cys Pro Pro Arg Ile
530 535 540
Asn Leu Lys Arg Glu Leu Asn Ser Lys
545

<210> 20
<211> 337
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1265980CD1

<400> 20
Met Leu Thr Leu Pro Phe Asp Glu Ser Val Val Met Pro Glu Ser
1 5 10 15
Gln Met Cys Arg Lys Phe Ser Arg Glu Cys Glu Asp Gln Lys Gln
20 25 30
Ile Lys Lys Pro Glu Ser Phe Ser Lys Gln Ile Val Leu Arg Gly
35 40 45
Lys Ser Ile Lys Arg Ala Pro Gly Glu Glu Thr Glu Lys Glu Glu
50 55 60
Glu Glu Glu Asp Arg Glu Glu Glu Asp Glu Asn Gly Leu Pro Arg
65 70 75
Arg Arg Gly Leu Arg Lys Lys Lys Thr Thr Lys Leu Arg Leu Glu
80 85 90
Arg Val Lys Phe Arg Arg Gln Glu Ala Asn Ala Arg Glu Arg Asn
95 100 105
Arg Met His Gly Leu Asn Asp Ala Leu Asp Asn Leu Arg Lys Val
110 115 120
Val Pro Cys Tyr Ser Arg Thr Gln Lys Leu Ser Lys Ile Glu Thr
125 130 135
Leu Arg Leu Ala Lys Asn Tyr Ile Trp Ala Leu Ser Glu Ile Leu
140 145 150
Arg Ile Gly Lys Arg Pro Asp Leu Leu Thr Phe Val Gln Asn Leu
155 160 165
Cys Lys Gly Leu Ser Gln Pro Thr Thr Asn Leu Val Ala Gly Cys
170 175 180
Leu Gln Leu Asn Ala Arg Ser Phe Leu Met Gly Gln Gly Gly Glu
185 190 195

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Ala Ala His His Thr Arg Ser Pro Tyr Ser Thr Phe Tyr Pro Pro
                200                 205                 210
Tyr His Ser Pro Glu Leu Thr Thr Pro Pro Gly His Gly Thr Leu
                215                 220                 225
Asp Asn Ser Lys Ser Met Lys Pro Tyr Asn Tyr Cys Ser Ala Tyr
                230                 235                 240
Glu Ser Phe Tyr Glu Ser Thr Ser Pro Glu Cys Ala Ser Pro Gln
                245                 250                 255
Phe Glu Gly Pro Leu Ser Pro Pro Pro Ile Asn Tyr Asn Gly Ile
                260                 265                 270
Phe Ser Leu Lys Gln Glu Glu Thr Leu Asp Tyr Gly Lys Asn Tyr
                275                 280                 285
Asn Tyr Gly Met His Tyr Cys Ala Val Pro Pro Arg Gly Pro Leu
                290                 295                 300
Gly Gln Gly Ala Met Phe Arg Leu Pro Thr Asp Ser His Phe Pro
                305                 310                 315
Tyr Asp Leu His Leu Arg Ser Gln Ser Leu Thr Met Gln Asp Glu
                320                 325                 330
Leu Asn Ala Val Phe His Asn
                335

<210> 21
<211> 581
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1297333CD1

<400> 21
Met Val Lys Arg Glu Leu Thr Gly Ser Leu Phe Ser Gly Gln Arg
 1               5                  10                  15
Ser Val His Glu Thr Gln Glu Leu Phe Pro Lys Gln Asp Ser Tyr
                20                  25                  30
Ala Glu Gly Val Thr Asp Arg Thr Ser Asn Thr Lys Leu Asp Cys
                35                  40                  45
Ser Ser Phe Arg Glu Asn Trp Asp Ser Asp Tyr Val Phe Gly Arg
                50                  55                  60
Lys Leu Ala Val Gly Gln Glu Thr Gln Phe Arg Gln Glu Pro Ile
                65                  70                  75
Thr His Asn Lys Thr Leu Ser Lys Glu Arg Glu Arg Thr Tyr Asn
                80                  85                  90
Lys Ser Gly Arg Trp Phe Tyr Leu Asp Asp Ser Glu Glu Lys Val
                95                  100                 105
His Asn Arg Asp Ser Ile Lys Asn Phe Gln Lys Ser Ser Val Val
                110                 115                 120
Ile Lys Gln Thr Gly Ile Tyr Ala Gly Lys Lys Leu Phe Lys Cys
                125                 130                 135
Asn Glu Cys Lys Lys Thr Phe Thr Gln Ser Ser Ser Leu Thr Val
                140                 145                 150
His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Asn Glu
                155                 160                 165
Cys Gly Lys Ala Phe Ser Asp Gly Ser Ser Phe Ala Arg His Gln
                170                 175                 180
Arg Cys His Thr Gly Lys Lys Pro Tyr Glu Cys Ile Glu Cys Gly
                185                 190                 195
Lys Ala Phe Ile Gln Asn Thr Ser Leu Ile Arg His Trp Arg Tyr
                200                 205                 210
Tyr His Thr Gly Glu Lys Pro Phe Asp Cys Ile Asp Cys Gly Lys
                215                 220                 225
Ala Phe Ser Asp His Ile Gly Leu Asn Gln His Arg Arg Ile His
                230                 235                 240
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```
Thr Gly Glu Lys Pro Tyr Lys Cys Asp Val Cys His Lys Ser Phe
                245                 250                 255
Arg Tyr Gly Ser Ser Leu Thr Val His Gln Arg Ile His Thr Gly
                260                 265                 270
Glu Lys Pro Tyr Glu Cys Asp Val Cys Arg Lys Ala Phe Ser His
                275                 280                 285
His Ala Ser Leu Thr Gln His Gln Arg Val His Ser Gly Glu Lys
                290                 295                 300
Pro Phe Lys Cys Lys Glu Cys Gly Lys Ala Phe Arg Gln Asn Ile
                305                 310                 315
His Leu Ala Ser His Leu Arg Ile His Thr Gly Glu Lys Pro Phe
                320                 325                 330
Glu Cys Ala Glu Cys Gly Lys Ser Phe Ser Ile Ser Ser Gln Leu
                335                 340                 345
Ala Thr His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys
                350                 355                 360
Lys Val Cys Ser Lys Ala Phe Thr Gln Lys Ala His Leu Ala Gln
                365                 370                 375
His Gln Lys Thr His Thr Gly Glu Lys Pro Tyr Glu Cys Lys Glu
                380                 385                 390
Cys Gly Lys Ala Phe Ser Gln Thr Thr His Leu Ile Gln His Gln
                395                 400                 405
Arg Val His Thr Gly Glu Lys Pro Tyr Lys Cys Met Glu Cys Gly
                410                 415                 420
Lys Ala Phe Gly Asp Asn Ser Ser Cys Thr Gln His Gln Arg Leu
                425                 430                 435
His Thr Gly Gln Arg Pro Tyr Glu Cys Ile Glu Cys Gly Lys Ala
                440                 445                 450
Phe Lys Thr Lys Ser Ser Leu Ile Cys His Arg Arg Ser His Thr
                455                 460                 465
Gly Glu Lys Pro Tyr Glu Cys Ser Val Cys Gly Lys Ala Phe Ser
                470                 475                 480
His Arg Gln Ser Leu Ser Val His Gln Arg Ile His Ser Gly Lys
                485                 490                 495
Lys Pro Tyr Glu Cys Lys Glu Cys Arg Lys Thr Phe Ile Gln Ile
                500                 505                 510
Gly His Leu Asn Gln His Lys Arg Val His Thr Gly Glu Arg Ser
                515                 520                 525
Tyr Asn Tyr Lys Lys Ser Arg Lys Val Phe Arg Gln Thr Ala His
                530                 535                 540
Leu Ala His His Gln Arg Ile His Thr Gly Glu Ser Ser Thr Cys
                545                 550                 555
Pro Ser Leu Pro Ser Thr Ser Asn Pro Val Asp Leu Phe Pro Lys
                560                 565                 570
Phe Leu Trp Asn Pro Ser Ser Leu Pro Ser Pro
                575                 580
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<210> 22
<211> 591
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1312824CD1

<400> 22

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Met Ala Ala Val Val Gln Gln Asn Asp Leu Val Phe Glu Phe Ala
 1               5                  10                  15
Ser Asn Val Met Glu Asp Glu Arg Gln Leu Gly Asp Pro Ala Ile
                20                  25                  30
Phe Pro Ala Val Ile Val Glu His Val Pro Gly Ala Asp Ile Leu
                35                  40                  45
```

```
Asn Ser Tyr Ala Gly Leu Ala Cys Val Glu Glu Pro Ser Asp Met
                50                  55                  60
Ile Thr Glu Ser Ser Leu Asp Val Ala Glu Glu Glu Ile Ile Asp
                65                  70                  75
Asp Asp Asp Asp Asp Ile Thr Leu Thr Val Glu Ala Ser Cys His
                80                  85                  90
Asp Gly Asp Glu Thr Ile Glu Thr Ile Glu Ala Ala Glu Ala Leu
                95                  100                 105
Leu Asn Met Asp Ser Pro Gly Pro Met Leu Asp Glu Lys Arg Ile
                110                 115                 120
Asn Asn Asn Ile Phe Ser Ser Pro Glu Asp Asp Met Val Val Ala
                125                 130                 135
Pro Val Thr His Val Ser Val Thr Leu Asp Gly Ile Pro Glu Val
                140                 145                 150
Met Glu Thr Gln Gln Val Gln Glu Lys Tyr Ala Asp Ser Pro Gly
                155                 160                 165
Ala Ser Ser Pro Glu Gln Pro Lys Arg Lys Lys Gly Asn Thr Ile
                170                 175                 180
Tyr Leu Trp Glu Phe Leu Leu Ala Leu Leu Gln Asp Lys Ala Thr
                185                 190                 195
Cys Pro Lys Tyr Ile Lys Trp Thr Gln Arg Glu Lys Gly Ile Phe
                200                 205                 210
Lys Leu Val Asp Ser Lys Ala Val Ser Arg Leu Trp Gly Lys His
                215                 220                 225
Lys Asn Lys Pro Asp Met Asn Tyr Glu Thr Met Gly Arg Ala Leu
                230                 235                 240
Arg Tyr Tyr Tyr Gln Arg Gly Ile Leu Ala Lys Val Glu Gly Gln
                245                 250                 255
Arg Leu Val Tyr Gln Phe Lys Glu Met Pro Lys Asp Leu Ile Tyr
                260                 265                 270
Ile Asn Asp Glu Asp Pro Ser Ser Ser Ile Glu Ser Ser Asp Pro
                275                 280                 285
Ser Leu Ser Ser Ser Ala Thr Ser Asn Arg Asn Gln Thr Ser Arg
                290                 295                 300
Ser Arg Val Ser Ser Ser Pro Gly Val Lys Gly Gly Ala Thr Ser
                305                 310                 315
Val Leu Lys Pro Gly Asn Ser Lys Ala Ala Lys Pro Lys Asp Pro
                320                 325                 330
Val Glu Val Ala Gln Pro Ser Glu Val Leu Arg Thr Val Gln Pro
                335                 340                 345
Thr Gln Ser Pro Tyr Pro Thr Gln Leu Phe Arg Thr Val His Val
                350                 355                 360
Val Gln Pro Val Gln Ala Val Pro Glu Gly Glu Ala Ala Arg Thr
                365                 370                 375
Ser Thr Met Gln Asp Glu Thr Leu Asn Ser Ser Val Gln Ser Ile
                380                 385                 390
Arg Thr Ile Gln Ala Pro Thr Gln Val Pro Val Val Val Ser Pro
                395                 400                 405
Arg Asn Gln Gln Leu His Thr Val Thr Leu Gln Thr Val Pro Leu
                410                 415                 420
Thr Thr Val Ile Ala Ser Thr Asp Pro Ser Ala Gly Thr Gly Ser
                425                 430                 435
Gln Lys Phe Ile Leu Gln Ala Ile Pro Ser Ser Gln Pro Met Thr
                440                 445                 450
Val Leu Lys Glu Asn Val Met Leu Gln Ser Gln Lys Ala Gly Ser
                455                 460                 465
Pro Pro Ser Ile Val Leu Gly Pro Ala Gln Val Gln Gln Val Leu
                470                 475                 480
Thr Ser Asn Val Gln Thr Ile Cys Asn Gly Thr Val Ser Val Ala
                485                 490                 495
Ser Ser Pro Ser Phe Ser Ala Thr Ala Pro Val Val Thr Phe Ser
                500                 505                 510
Pro Arg Ser Ser Gln Leu Val Ala His Pro Pro Gly Thr Val Ile
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                515                     520                     525
Thr Ser Val Ile Lys Thr Gln Glu Thr Lys Thr Leu Thr Gln Glu
                530                     535                     540
Val Glu Lys Lys Glu Ser Glu Asp His Leu Lys Glu Asn Thr Glu
                545                     550                     555
Lys Thr Glu Gln Gln Pro Gln Pro Tyr Val Met Val Val Ser Ser
                560                     565                     570
Ser Asn Gly Phe Thr Ser Gln Val Ala Met Lys Gln Asn Glu Leu
                575                     580                     585
Leu Glu Pro Asn Ser Phe
                590

<210> 23
<211> 767
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1359294CD1

<400> 23
Met Ser Phe Asp Pro Asn Leu Leu His Asn Asn Gly His Asn Gly
  1               5                  10                  15
Tyr Pro Asn Gly Thr Ser Ala Ala Leu Arg Glu Thr Gly Val Ile
                 20                  25                  30
Glu Lys Leu Leu Thr Ser Tyr Gly Phe Ile Gln Cys Ser Glu Arg
                 35                  40                  45
Gln Ala Arg Leu Phe Phe His Cys Ser Gln Tyr Asn Gly Asn Leu
                 50                  55                  60
Gln Asp Leu Lys Val Gly Asp Asp Val Glu Phe Glu Val Ser Ser
                 65                  70                  75
Asp Arg Arg Thr Gly Lys Pro Ile Ala Val Lys Leu Val Lys Ile
                 80                  85                  90
Lys Gln Glu Ile Leu Pro Glu Glu Arg Met Asn Gly Gln Glu Val
                 95                 100                 105
Phe Tyr Leu Thr Tyr Thr Pro Glu Asp Val Glu Gly Asn Val Gln
                110                 115                 120
Leu Glu Thr Gly Asp Lys Ile Asn Phe Val Ile Asp Asn Asn Lys
                125                 130                 135
His Thr Gly Ala Val Ser Ala Arg Asn Ile Met Leu Leu Lys Lys
                140                 145                 150
Lys Gln Ala Arg Cys Gln Gly Val Val Cys Ala Met Lys Glu Ala
                155                 160                 165
Phe Gly Phe Ile Glu Arg Gly Asp Val Val Lys Glu Ile Phe Phe
                170                 175                 180
His Tyr Ser Glu Phe Lys Gly Asp Leu Glu Thr Leu Gln Pro Gly
                185                 190                 195
Asp Asp Val Glu Phe Thr Ile Lys Asp Arg Asn Gly Lys Glu Val
                200                 205                 210
Ala Thr Asp Val Arg Leu Leu Pro Gln Gly Thr Val Ile Phe Glu
                215                 220                 225
Asp Ile Ser Ile Glu His Phe Glu Gly Thr Val Thr Lys Val Ile
                230                 235                 240
Pro Lys Val Pro Ser Lys Asn Gln Asn Asp Pro Leu Pro Gly Arg
                245                 250                 255
Ile Lys Val Asp Phe Val Ile Pro Lys Glu Leu Pro Phe Gly Asp
                260                 265                 270
Lys Asp Thr Lys Ser Lys Val Thr Leu Leu Glu Gly Asp His Val
                275                 280                 285
Arg Phe Asn Ile Ser Thr Asp Arg Arg Asp Lys Leu Glu Arg Ala
                290                 295                 300
Thr Asn Ile Glu Val Leu Ser Asn Thr Phe Gln Phe Thr Asn Glu
```

305 310 315
Ala Arg Glu Met Gly Val Ile Ala Ala Met Arg Asp Gly Phe Gly
320 325 330
Phe Ile Lys Cys Val Asp Arg Asp Val Arg Met Phe Phe His Phe
335 340 345
Ser Glu Ile Leu Asp Gly Asn Gln Leu His Ile Ala Asp Glu Val
350 355 360
Glu Phe Thr Val Val Pro Asp Met Leu Ser Ala Gln Arg Asn His
365 370 375
Ala Ile Arg Ile Lys Lys Leu Pro Lys Gly Thr Val Ser Phe His
380 385 390
Ser His Ser Asp His Arg Phe Leu Gly Thr Val Glu Lys Glu Ala
395 400 405
Thr Phe Ser Asn Pro Lys Thr Thr Ser Pro Asn Lys Gly Lys Glu
410 415 420
Lys Glu Ala Glu Asp Gly Ile Ile Ala Tyr Asp Asp Cys Gly Val
425 430 435
Lys Leu Thr Ile Ala Phe Gln Ala Lys Asp Val Glu Gly Ser Thr
440 445 450
Ser Pro Gln Ile Gly Asp Lys Val Glu Phe Ser Ile Ser Asp Lys
455 460 465
Gln Arg Pro Gly Gln Gln Val Ala Thr Cys Val Arg Leu Leu Gly
470 475 480
Arg Asn Ser Asn Ser Lys Arg Leu Leu Gly Tyr Val Ala Thr Leu
485 490 495
Lys Asp Asn Phe Gly Phe Ile Glu Thr Ala Asn His Asp Lys Glu
500 505 510
Ile Phe Phe His Tyr Ser Glu Phe Ser Gly Asp Val Asp Ser Leu
515 520 525
Glu Leu Gly Asp Met Val Glu Tyr Ser Leu Ser Lys Gly Lys Gly
530 535 540
Asn Lys Val Ser Ala Glu Lys Val Asn Lys Thr His Ser Val Asn
545 550 555
Gly Ile Thr Glu Glu Ala Asp Pro Thr Ile Tyr Ser Gly Lys Val
560 565 570
Ile Arg Pro Leu Arg Ser Val Asp Pro Thr Gln Thr Glu Tyr Gln
575 580 585
Gly Met Ile Glu Ile Val Glu Glu Gly Asp Met Lys Gly Glu Val
590 595 600
Tyr Pro Phe Gly Ile Val Gly Met Ala Asn Lys Gly Asp Cys Leu
605 610 615
Gln Lys Gly Glu Ser Val Lys Phe Gln Leu Cys Val Leu Gly Gln
620 625 630
Asn Ala Gln Thr Met Ala Tyr Asn Ile Thr Pro Leu Arg Arg Ala
635 640 645
Thr Val Glu Cys Val Lys Asp Gln Phe Gly Phe Ile Asn Tyr Glu
650 655 660
Val Gly Asp Ser Lys Lys Leu Phe Phe His Val Lys Glu Val Gln
665 670 675
Asp Gly Ile Glu Leu Gln Ala Gly Asp Glu Val Glu Phe Ser Val
680 685 690
Ile Leu Asn Gln Arg Thr Gly Lys Cys Ser Ala Cys Asn Val Trp
695 700 705
Arg Val Cys Glu Gly Pro Lys Ala Val Ala Ala Pro Arg Pro Asp
710 715 720
Arg Leu Val Asn Arg Leu Lys Asn Ile Thr Leu Asp Asp Ala Ser
725 730 735
Ala Pro Arg Leu Met Val Leu Arg Gln Pro Arg Gly Pro Asp Asn
740 745 750
Ser Met Gly Phe Gly Ala Glu Arg Lys Ile Arg Gln Ala Gly Val
755 760 765
Ile Asp

<210> 24
<211> 206
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1377380CD1

<400> 24
Met Ser Pro Arg Lys Ala Leu Ile Pro Val Ser Gln Lys Ser Ser
1 5 10 15
Gln Ala Glu Ala Cys Ser Glu Ser Arg Asn Arg Val Lys Arg Arg
20 25 30
Leu Asp Ser Ser Cys Leu Glu Ser Val Lys Gln Lys Cys Val Lys
35 40 45
Ser Cys Asn Cys Val Thr Glu Leu Asp Gly Gln Val Glu Asn Leu
50 55 60
His Leu Asp Leu Cys Cys Leu Ala Gly Asn Gln Glu Asp Leu Ser
65 70 75
Lys Asp Ser Leu Gly Pro Thr Lys Ser Ser Lys Ile Glu Gly Ala
80 85 90
Gly Thr Ser Ile Ser Glu Pro Pro Ser Pro Ile Ser Pro Tyr Ala
95 100 105
Ser Glu Ser Cys Gly Thr Leu Pro Leu Pro Leu Arg Pro Cys Gly
110 115 120
Glu Gly Ser Glu Met Val Gly Lys Glu Asn Ser Ser Pro Glu Asn
125 130 135
Lys Asn Trp Leu Leu Ala Met Ala Ala Lys Arg Lys Ala Glu Asn
140 145 150
Pro Ser Pro Arg Ser Pro Ser Ser Gln Thr Pro Asn Ser Arg Arg
155 160 165
Gln Ser Gly Lys Thr Leu Pro Ser Pro Val Thr Ile Thr Pro Ser
170 175 180
Ser Met Arg Lys Ile Cys Thr Tyr Phe His Arg Lys Ser Gln Glu
185 190 195
Asp Phe Cys Gly Pro Glu His Ser Thr Glu Leu
200 205

<210> 25
<211> 352
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1383473CD1

<400> 25
Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu
1 5 10 15
Gly Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg
20 25 30
Gln Lys Ala Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val
35 40 45
His Leu Gly Glu Asp Leu Lys Ser Ile Leu Ser Glu Ala Pro Gly
50 55 60
Lys Cys Val Pro Tyr Ala Val Ile Glu Gly Ala Val Arg Ser Val
65 70 75
Lys Glu Thr Leu Asn Ser Gln Phe Val Glu Asn Cys Lys Gly Val
80 85 90
Ile Gln Arg Leu Thr Leu Gln Glu His Lys Met Val Trp Asn Arg
95 100 105

Thr Thr His Leu Trp Asn Asp Cys Ser Lys Ile Ile His Gln Arg
110 115 120
Thr Asn Thr Val Pro Phe Asp Leu Val Pro His Glu Asp Gly Val
125 130 135
Asp Val Ala Val Arg Val Leu Lys Pro Leu Asp Ser Val Asp Leu
140 145 150
Gly Leu Glu Thr Val Tyr Glu Lys Phe His Pro Ser Ile Gln Ser
155 160 165
Phe Thr Asp Val Ile Gly His Tyr Ile Ser Gly Glu Arg Pro Lys
170 175 180
Gly Ile Gln Glu Thr Glu Glu Met Leu Lys Val Gly Ala Thr Leu
185 190 195
Thr Gly Val Gly Glu Leu Val Leu Asp Asn Asn Ser Val Arg Leu
200 205 210
Gln Pro Pro Lys Gln Gly Met Gln Tyr Tyr Leu Ser Ser Gln Asp
215 220 225
Phe Asp Ser Leu Leu Gln Arg Gln Glu Ser Ser Val Arg Leu Trp
230 235 240
Lys Val Leu Ala Leu Val Phe Gly Phe Ala Thr Cys Ala Thr Leu
245 250 255
Phe Phe Ile Leu Arg Lys Gln Tyr Leu Gln Arg Gln Glu Arg Leu
260 265 270
Arg Leu Lys Gln Met Gln Glu Glu Phe Gln Glu His Glu Ala Gln
275 280 285
Leu Leu Ser Arg Ala Lys Pro Glu Asp Arg Glu Ser Leu Lys Ser
290 295 300
Ala Cys Val Val Cys Leu Ser Ser Phe Lys Ser Cys Val Phe Leu
305 310 315
Glu Cys Gly His Val Cys Ser Cys Thr Glu Cys Tyr Arg Ala Leu
320 325 330
Pro Glu Pro Lys Lys Cys Pro Ile Cys Arg Gln Ala Ile Thr Arg
335 340 345
Val Ile Pro Leu Tyr Asn Ser
350

<210> 26
<211> 532
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1388860CD1

<400> 26
Met Met Phe Gln Asp Ser Val Ala Phe Glu Asp Val Ala Val Ser
1 5 10 15
Phe Thr Gln Glu Glu Trp Ala Leu Leu Asp Pro Ser Gln Lys Asn
20 25 30
Leu Tyr Arg Asp Val Met Gln Glu Thr Phe Lys Asn Leu Thr Ser
35 40 45
Val Gly Lys Thr Trp Lys Val Gln Asn Ile Glu Asp Glu Tyr Lys
50 55 60
Asn Pro Arg Arg Asn Leu Ser Leu Met Arg Glu Lys Leu Cys Glu
65 70 75
Ser Lys Glu Ser His His Cys Gly Glu Ser Phe Asn Gln Ile Ala
80 85 90
Asp Asp Met Leu Asn Arg Lys Thr Leu Pro Gly Ile Thr Pro Cys
95 100 105
Glu Ser Ser Val Cys Gly Glu Val Gly Thr Gly His Ser Ser Leu
110 115 120
Asn Thr His Ile Arg Ala Asp Thr Gly His Lys Ser Ser Glu Tyr
125 130 135

```
Gln Glu Tyr Gly Glu Asn Pro Tyr Arg Asn Lys Glu Cys Lys Lys
                140                 145                 150
Ala Phe Ser Tyr Leu Asp Ser Leu Gln Ser His Asp Lys Ala Cys
                155                 160                 165
Thr Lys Glu Lys Pro Tyr Asp Gly Lys Glu Cys Thr Glu Thr Phe
                170                 175                 180
Ile Ser His Ser Cys Ile Gln Arg His Arg Val Met His Ser Gly
                185                 190                 195
Asp Gly Pro Tyr Lys Cys Lys Phe Cys Gly Lys Ala Phe Tyr Phe
                200                 205                 210
Leu Asn Leu Cys Leu Ile His Glu Arg Ile His Thr Gly Val Lys
                215                 220                 225
Pro Tyr Lys Cys Lys Gln Cys Gly Lys Ala Phe Thr Arg Ser Thr
                230                 235                 240
Thr Leu Pro Val His Glu Arg Thr His Thr Gly Val Asn Ala Asp
                245                 250                 255
Glu Cys Lys Glu Cys Gly Asn Ala Phe Ser Phe Pro Ser Glu Ile
                260                 265                 270
Arg Arg His Lys Arg Ser His Thr Gly Glu Lys Pro Tyr Glu Cys
                275                 280                 285
Lys Gln Cys Gly Lys Val Phe Ile Ser Phe Ser Ser Ile Gln Tyr
                290                 295                 300
His Lys Met Thr His Thr Gly Glu Lys Pro Tyr Glu Cys Lys Gln
                305                 310                 315
Cys Gly Lys Ala Phe Arg Cys Gly Ser His Leu Gln Lys His Gly
                320                 325                 330
Arg Thr His Thr Gly Glu Lys Pro Tyr Glu Cys Arg Gln Cys Gly
                335                 340                 345
Lys Ala Phe Arg Cys Thr Ser Asp Leu Gln Arg His Glu Lys Thr
                350                 355                 360
His Thr Glu Asp Lys Pro Tyr Gly Cys Lys Gln Cys Gly Lys Gly
                365                 370                 375
Phe Arg Cys Ala Ser Gln Leu Gln Ile His Glu Arg Thr His Ser
                380                 385                 390
Gly Glu Lys Pro His Glu Cys Lys Glu Cys Gly Lys Val Phe Lys
                395                 400                 405
Tyr Phe Ser Ser Leu Arg Ile His Glu Arg Thr His Thr Gly Glu
                410                 415                 420
Lys Pro His Glu Cys Lys Gln Cys Gly Lys Ala Phe Arg Tyr Phe
                425                 430                 435
Ser Ser Leu His Ile His Glu Arg Thr His Thr Gly Asp Lys Pro
                440                 445                 450
Tyr Glu Cys Lys Val Cys Gly Lys Ala Phe Thr Cys Ser Ser Ser
                455                 460                 465
Ile Arg Tyr His Glu Arg Thr His Thr Gly Glu Lys Pro Tyr Glu
                470                 475                 480
Cys Lys His Cys Gly Lys Ala Phe Ile Ser Asn Tyr Ile Arg Tyr
                485                 490                 495
His Glu Arg Thr His Thr Gly Glu Lys Pro Tyr Gln Cys Lys Gln
                500                 505                 510
Cys Gly Lys Ala Phe Ile Arg Ala Ser Ser Cys Arg Glu His Glu
                515                 520                 525
Arg Thr His Thr Ile Asn Arg
                530
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<210> 27
<211> 444
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1395322CD1

<400> 27

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Met Glu Arg Tyr Leu Ser Thr Thr Pro Glu Thr Thr His Cys Arg
 1               5                  10                  15
Lys Gln Pro Arg Pro Val Arg Ile Gln Thr Leu Val Gly Asn Ile
                20                  25                  30
His Ile Lys Gln Glu Met Glu Asp Asp Tyr Asp Tyr Tyr Gly Gln
                35                  40                  45
Gln Arg Val Gln Ile Leu Glu Arg Asn Glu Ser Glu Glu Cys Thr
                50                  55                  60
Glu Asp Thr Asp Gln Ala Glu Gly Thr Glu Ser Glu Pro Lys Gly
                65                  70                  75
Glu Ser Phe Asp Ser Gly Val Ser Ser Ser Ile Gly Thr Glu Pro
                80                  85                  90
Asp Ser Val Glu Gln Gln Phe Gly Pro Gly Ala Ala Arg Asp Ser
                95                 100                 105
Gln Ala Glu Pro Thr Gln Pro Glu Gln Ala Ala Glu Ala Pro Ala
               110                 115                 120
Glu Gly Gly Pro Gln Thr Asn Gln Leu Glu Thr Gly Ala Ser Ser
               125                 130                 135
Pro Glu Arg Ser Asn Glu Val Glu Met Asp Ser Thr Val Ile Thr
               140                 145                 150
Val Ser Asn Ser Ser Asp Lys Ser Val Leu Gln Gln Pro Ser Val
               155                 160                 165
Asn Thr Ser Ile Gly Gln Pro Leu Pro Ser Thr Gln Leu Tyr Leu
               170                 175                 180
Arg Gln Thr Glu Thr Leu Thr Ser Asn Leu Arg Met Pro Leu Thr
               185                 190                 195
Leu Thr Ser Asn Thr Gln Val Ile Gly Thr Ala Gly Asn Thr Tyr
               200                 205                 210
Leu Pro Ala Leu Phe Thr Thr Gln Pro Ala Gly Ser Gly Pro Lys
               215                 220                 225
Pro Phe Leu Phe Ser Leu Pro Gln Pro Leu Ala Gly Gln Gln Thr
               230                 235                 240
Gln Phe Val Thr Val Ser Gln Pro Gly Leu Ser Thr Phe Thr Ala
               245                 250                 255
Gln Leu Pro Ala Pro Gln Pro Leu Ala Ser Ser Ala Gly His Ser
               260                 265                 270
Thr Ala Ser Gly Gln Gly Glu Lys Lys Pro Tyr Glu Cys Thr Leu
               275                 280                 285
Cys Asn Lys Thr Phe Thr Ala Lys Gln Asn Tyr Val Lys His Met
               290                 295                 300
Phe Val His Thr Gly Glu Lys Pro His Gln Cys Ser Ile Cys Trp
               305                 310                 315
Arg Ser Phe Ser Leu Lys Asp Tyr Leu Ile Lys Leu Met Val Thr
               320                 325                 330
His Thr Gly Val Arg Ala Tyr Gln Cys Ser Ile Cys Asn Lys Arg
               335                 340                 345
Phe Thr Gln Lys Ser Ser Leu Asn Val His Met Arg Leu His Arg
               350                 355                 360
Gly Glu Lys Ser Tyr Glu Cys Tyr Ile Cys Lys Lys Lys Phe Ser
               365                 370                 375
His Lys Thr Leu Leu Glu Arg His Val Ala Leu His Ser Ala Ser
               380                 385                 390
Asn Gly Thr Pro Pro Ala Gly Thr Pro Pro Gly Ala Arg Ala Gly
               395                 400                 405
Pro Pro Gly Val Val Ala Cys Thr Glu Gly Thr Thr Tyr Val Cys
               410                 415                 420
Ser Val Cys Pro Ala Lys Phe Asp Gln Ile Glu Gln Phe Asn Asp
               425                 430                 435
His Met Arg Met His Val Ser Asp Gly
               440
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<210> 28

<211> 347
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1419370CD1

<400> 28
Met Ser Phe Val Leu Ser Arg Met Ala Ala Cys Gly Gly Thr Cys
1 5 10 15
Lys Asn Lys Val Thr Val Ser Lys Pro Val Trp Asp Phe Leu Ser
20 25 30
Lys Glu Thr Pro Ala Arg Leu Ala Arg Leu Arg Glu Glu His Arg
35 40 45
Val Ser Ile Leu Ile Asp Gly Glu Thr Ser Asp Ile Tyr Val Leu
50 55 60
Gln Leu Ser Pro Gln Gly Pro Pro Pro Ala Pro Pro Asn Gly Leu
65 70 75
Tyr Leu Ala Arg Lys Ala Leu Lys Gly Leu Leu Lys Glu Ala Glu
80 85 90
Lys Glu Leu Lys Lys Ala Gln Arg Gln Gly Glu Leu Met Gly Cys
95 100 105
Leu Ala Leu Gly Gly Gly Gly Glu His Pro Glu Met His Arg Ala
110 115 120
Gly Pro Pro Pro Leu Arg Ala Ala Pro Leu Leu Pro Pro Gly Ala
125 130 135
Arg Gly Leu Pro Pro Pro Pro Pro Pro Leu Pro Pro Pro Leu Pro
140 145 150
Pro Arg Leu Arg Glu Glu Ala Glu Glu Gln Glu Ser Thr Cys Pro
155 160 165
Ile Cys Leu Gly Glu Ile Gln Asn Ala Lys Thr Leu Glu Lys Cys
170 175 180
Arg His Ser Phe Cys Glu Gly Cys Ile Thr Arg Ala Leu Gln Val
185 190 195
Lys Lys Ala Cys Pro Met Cys Gly Arg Phe Tyr Gly Gln Leu Val
200 205 210
Gly Asn Gln Pro Gln Asn Gly Arg Met Leu Val Ser Lys Asp Ala
215 220 225
Thr Leu Leu Leu Pro Ser Tyr Glu Lys Tyr Gly Thr Ile Val Ile
230 235 240
Gln Tyr Val Phe Pro Pro Gly Val Gln Gly Ala Glu His Pro Asn
245 250 255
Pro Gly Val Arg Tyr Pro Gly Thr Thr Arg Val Ala Tyr Leu Pro
260 265 270
Asp Cys Pro Glu Gly Asn Lys Val Leu Thr Leu Phe Arg Lys Ala
275 280 285
Phe Asp Gln Arg Leu Thr Phe Thr Ile Gly Thr Ser Met Thr Thr
290 295 300
Gly Arg Pro Asn Val Ile Thr Trp Asn Asp Ile His His Lys Thr
305 310 315
Ser Cys Thr Gly Gly Pro Gln Leu Phe Gly Tyr Pro Asp Pro Thr
320 325 330
Tyr Leu Thr Arg Val Gln Glu Glu Leu Arg Ala Lys Gly Ile Thr
335 340 345
Asp Asp

<210> 29
<211> 308
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1429773CD1

<400> 29
Met Gln Pro Ser Gly His Arg Leu Arg Asp Val Glu His His Pro
1 5 10 15
Leu Leu Ala Glu Asn Asp Asn Tyr Asp Ser Ser Ser Ser Ser Ser
20 25 30
Ser Glu Ala Asp Val Ala Asp Arg Val Trp Phe Ile Arg Asp Gly
35 40 45
Cys Gly Met Ile Cys Ala Val Met Thr Trp Leu Leu Val Ala Tyr
50 55 60
Ala Asp Phe Val Val Thr Phe Val Met Leu Leu Pro Ser Lys Asp
65 70 75
Phe Trp Tyr Ser Val Val Asn Gly Val Ile Phe Asn Cys Leu Ala
80 85 90
Val Leu Ala Leu Ser Ser His Leu Arg Thr Met Leu Thr Asp Pro
95 100 105
Gly Ala Val Pro Lys Gly Asn Ala Thr Lys Glu Tyr Met Glu Ser
110 115 120
Leu Gln Leu Lys Pro Gly Glu Val Ile Tyr Lys Cys Pro Lys Cys
125 130 135
Cys Cys Ile Lys Pro Glu Arg Ala His His Cys Ser Ile Cys Lys
140 145 150
Arg Cys Ile Arg Lys Met Asp His His Cys Pro Trp Val Asn Asn
155 160 165
Cys Val Gly Glu Lys Asn Gln Arg Phe Phe Val Leu Phe Thr Met
170 175 180
Tyr Ile Ala Leu Ser Ser Val His Ala Leu Ile Leu Cys Gly Phe
185 190 195
Gln Phe Ile Ser Cys Val Arg Gly Gln Trp Thr Glu Cys Ser Asp
200 205 210
Phe Ser Pro Pro Ile Thr Val Ile Leu Leu Ile Phe Leu Cys Leu
215 220 225
Glu Gly Leu Leu Phe Phe Thr Phe Thr Ala Val Met Phe Gly Thr
230 235 240
Gln Ile His Ser Ile Cys Asn Asp Glu Thr Glu Ile Glu Arg Leu
245 250 255
Lys Ser Glu Lys Pro Thr Trp Glu Arg Arg Leu Arg Trp Glu Gly
260 265 270
Met Lys Ser Val Phe Gly Gly Pro Pro Ser Leu Leu Trp Met Asn
275 280 285
Pro Phe Val Gly Phe Arg Phe Arg Arg Leu Pro Thr Arg Pro Arg
290 295 300
Lys Gly Gly Pro Glu Phe Ser Val
305

<210> 30
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1470820CD1

<400> 30
Met Cys Tyr Ile Tyr Pro Phe Val Phe Leu Arg Leu Asp Ser Met
1 5 10 15
Lys Glu Leu His Lys Thr Asn Arg Gln Gln His Glu Lys His Leu
20 25 30
Gln Ser Arg Val Asp Ser Thr Arg Ala Ile Glu Arg Leu Glu Gly

```
                35                  40                  45
Ser Ser Gly Gly Ile Gly Glu Arg Tyr Lys Phe Leu Gln Glu Met
                50                  55                  60
Arg Gly Tyr Val Gln Asp Leu Leu Glu Cys Phe Ser Glu Lys Val
                65                  70                  75
Arg Met Gln Lys Tyr
                80

<210> 31
<211> 570
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1483455CD1

<400> 31
Met Pro Gln Val Thr Phe Asn Asp Val Ala Ile Asp Phe Thr His
  1               5                  10                  15
Glu Glu Trp Gly Trp Leu Ser Ser Ala Gln Arg Asp Leu Tyr Lys
                20                  25                  30
Asp Val Met Val Gln Asn Tyr Glu Asn Leu Val Ser Val Gly Leu
                35                  40                  45
Ser Val Thr Lys Pro Tyr Val Ile Thr Leu Leu Glu Asp Gly Lys
                50                  55                  60
Glu Pro Trp Met Met Glu Lys Lys Leu Ser Lys Gly Met Ile Pro
                65                  70                  75
Asp Trp Glu Ser Arg Trp Glu Asn Lys Glu Leu Ser Thr Lys Lys
                80                  85                  90
Asp Asn Tyr Asp Glu Asp Ser Pro Gln Thr Val Ile Ile Glu Lys
                95                 100                 105
Val Val Lys Gln Ser Tyr Glu Phe Ser Asn Ser Lys Lys Asn Leu
               110                 115                 120
Glu Tyr Ile Glu Lys Leu Glu Gly Lys His Gly Ser Gln Val Asp
               125                 130                 135
His Phe Arg Pro Ala Ile Leu Thr Ser Arg Glu Ser Pro Thr Ala
               140                 145                 150
Asp Ser Val Tyr Lys Tyr Asn Ile Phe Arg Ser Thr Phe His Ser
               155                 160                 165
Lys Ser Thr Leu Ser Glu Pro Gln Lys Ile Ser Ala Glu Gly Asn
               170                 175                 180
Ser His Lys Tyr Asp Ile Leu Lys Lys Asn Leu Pro Lys Lys Ser
               185                 190                 195
Val Ile Lys Asn Glu Lys Val Asn Gly Gly Lys Lys Leu Leu Asn
               200                 205                 210
Ser Asn Lys Ser Gly Ala Ala Phe Ser Gln Gly Lys Ser Leu Thr
               215                 220                 225
Leu Pro Gln Thr Cys Asn Arg Glu Lys Ile Tyr Thr Cys Ser Glu
               230                 235                 240
Cys Gly Lys Ala Phe Gly Lys Gln Ser Ile Leu Asn Arg His Trp
               245                 250                 255
Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Arg Glu Cys Gly
               260                 265                 270
Lys Thr Phe Ser His Gly Ser Ser Leu Thr Arg His Leu Ile Ser
               275                 280                 285
His Ser Gly Glu Lys Pro Tyr Lys Cys Ile Glu Cys Gly Lys Ala
               290                 295                 300
Phe Ser His Val Ser Ser Leu Thr Asn His Gln Ser Thr His Thr
               305                 310                 315
Gly Glu Lys Pro Tyr Glu Cys Met Asn Cys Gly Lys Ser Phe Ser
               320                 325                 330
Arg Val Ser His Leu Ile Glu His Leu Arg Ile His Thr Gln Glu
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                335                 340                 345
Lys Leu Tyr Glu Cys Arg Ile Cys Gly Lys Ala Phe Ile His Arg
                350                 355                 360
Ser Ser Leu Ile His His Gln Lys Ile His Thr Gly Glu Lys Pro
                365                 370                 375
Tyr Glu Cys Arg Glu Cys Gly Lys Ala Phe Cys Cys Ser Ser His
                380                 385                 390
Leu Thr Arg His Gln Arg Ile His Thr Met Glu Lys Gln Tyr Glu
                395                 400                 405
Cys Asn Lys Cys Leu Lys Val Phe Ser Ser Leu Ser Phe Leu Val
                410                 415                 420
Gln His Gln Ser Ile His Thr Glu Glu Lys Pro Phe Glu Cys Gln
                425                 430                 435
Lys Cys Arg Lys Ser Phe Asn Gln Leu Glu Ser Leu Asn Met His
                440                 445                 450
Leu Arg Asn His Ile Arg Leu Lys Pro Tyr Glu Cys Ser Ile Cys
                455                 460                 465
Gly Lys Ala Phe Ser His Arg Ser Ser Leu Leu Gln His His Arg
                470                 475                 480
Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Ile Lys Cys Gly Lys
                485                 490                 495
Thr Phe Ser Cys Ser Ser Asn Leu Thr Val His Gln Arg Ile His
                500                 505                 510
Thr Gly Glu Lys Pro Tyr Lys Cys Asn Glu Cys Gly Lys Ala Phe
                515                 520                 525
Ser Lys Gly Ser Asn Leu Thr Ala His Gln Arg Val His Asn Gly
                530                 535                 540
Glu Lys Pro Asn Ser Val Val Ser Val Glu Lys Pro Leu Asp Tyr
                545                 550                 555
Met Asn His Tyr Thr Cys Glu Lys Ser Tyr Arg Arg Glu Thr Val
                560                 565                 570


<210> 32
<211> 390
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1527064CD1

<400> 32
Met Arg Gly Asp Arg Gly Arg Gly Arg Gly Gly Arg Phe Gly Ser
  1               5                  10                  15
Arg Gly Gly Pro Gly Gly Gly Phe Arg Pro Phe Val Pro His Ile
                 20                  25                  30
Pro Phe Asp Phe Tyr Leu Cys Glu Met Ala Phe Pro Arg Val Lys
                 35                  40                  45
Pro Ala Pro Asp Glu Thr Ser Phe Ser Glu Ala Leu Leu Lys Arg
                 50                  55                  60
Asn Gln Asp Leu Ala Pro Asn Ser Ala Glu Gln Ala Ser Ile Leu
                 65                  70                  75
Ser Leu Val Thr Lys Ile Asn Asn Val Ile Asp Asn Leu Ile Val
                 80                  85                  90
Ala Pro Gly Thr Phe Glu Val Gln Ile Glu Glu Val Arg Gln Val
                 95                 100                 105
Gly Ser Tyr Lys Lys Gly Thr Met Thr Thr Gly His Asn Val Ala
                110                 115                 120
Asp Leu Val Val Ile Leu Lys Ile Leu Pro Thr Leu Glu Ala Val
                125                 130                 135
Ala Ala Leu Gly Asn Lys Val Val Glu Ser Leu Arg Ala Gln Asp
                140                 145                 150
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Pro Ser Glu Val Leu Thr Met Leu Thr Asn Glu Thr Gly Phe Glu
155 160 165
Ile Ser Ser Ser Asp Ala Thr Val Lys Ile Leu Ile Thr Thr Val
170 175 180
Pro Pro Asn Leu Arg Lys Leu Asp Pro Glu Leu His Leu Asp Ile
185 190 195
Lys Val Leu Gln Ser Ala Leu Ala Ala Ile Arg His Ala Arg Trp
200 205 210
Phe Glu Glu Asn Ala Ser Gln Ser Thr Val Lys Val Leu Ile Arg
215 220 225
Leu Leu Lys Asp Leu Arg Ile Arg Phe Pro Gly Phe Glu Pro Leu
230 235 240
Thr Pro Trp Ile Leu Asp Leu Leu Gly His Tyr Ala Val Met Asn
245 250 255
Asn Pro Thr Arg Gln Pro Leu Ala Leu Asn Val Ala Tyr Arg Arg
260 265 270
Cys Leu Gln Ile Leu Ala Ala Gly Leu Phe Leu Pro Gly Ser Val
275 280 285
Gly Ile Thr Asp Pro Cys Glu Ser Gly Asn Phe Arg Val His Thr
290 295 300
Val Met Thr Leu Glu Gln Gln Asp Met Val Cys Tyr Thr Ala Gln
305 310 315
Thr Leu Val Arg Ile Leu Ser His Gly Gly Phe Arg Lys Ile Leu
320 325 330
Gly Gln Glu Gly Asp Ala Ser Tyr Leu Ala Ser Glu Ile Ser Thr
335 340 345
Trp Asp Gly Val Ile Val Thr Pro Ser Glu Lys Ala Tyr Glu Lys
350 355 360
Pro Pro Glu Lys Lys Glu Gly Glu Glu Glu Glu Glu Asn Thr Glu
365 370 375
Glu Pro Pro Gln Gly Glu Glu Glu Glu Ser Met Glu Thr Gln Glu
380 385 390

<210> 33
<211> 601
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1557491CD1

<400> 33
Met Asn Glu Ser Ala Pro Gly Thr Tyr Val Val Gln Asn Pro His
1 5 10 15
Ser Ser Glu Leu Pro Thr Leu Asn Phe Gln Asp Thr Val Asn Thr
20 25 30
Leu Thr Asn Ser Pro Ala Ile Pro Leu Glu Thr Ser Ala Cys Gln
35 40 45
Asp Ile Pro Thr Ser Ala Asn Val Gln Asn Ala Glu Gly Thr Lys
50 55 60
Trp Gly Glu Glu Ala Leu Lys Met Asp Leu Asp Asn Asn Phe Tyr
65 70 75
Ser Thr Glu Val Ser Val Ser Ser Thr Glu Asn Ala Val Ser Ser
80 85 90
Asp Leu Arg Ala Gly Asp Val Pro Val Leu Ser Leu Ser Asn Ser
95 100 105
Ser Glu Asn Ala Ala Ser Val Ile Ser Tyr Ser Gly Ser Ala Pro
110 115 120
Ser Val Ile Val His Ser Ser Gln Phe Ser Ser Val Ile Met His
125 130 135
Ser Asn Ala Ile Ala Ala Met Thr Ser Ser Asn His Arg Ala Phe

140 145 150
Ser Asp Pro Ala Val Ser Gln Ser Leu Lys Asp Asp Ser Lys Pro
155 160 165
Glu Pro Asp Lys Val Gly Arg Phe Ala Ser Arg Pro Lys Ser Ile
170 175 180
Lys Glu Lys Lys Lys Thr Thr Ser His Thr Arg Gly Glu Ile Pro
185 190 195
Glu Glu Ser Asn Tyr Val Ala Asp Pro Gly Gly Ser Leu Ser Lys
200 205 210
Thr Thr Asn Ile Ala Glu Glu Thr Ser Lys Ile Glu Thr Tyr Ile
215 220 225
Ala Lys Pro Ala Leu Pro Gly Thr Ser Thr Asn Ser Asn Val Ala
230 235 240
Pro Leu Cys Gln Ile Thr Val Lys Ile Gly Asn Glu Ala Ile Val
245 250 255
Lys Arg His Ile Leu Gly Ser Lys Leu Phe Tyr Lys Arg Gly Arg
260 265 270
Arg Pro Lys Tyr Gln Met Gln Glu Glu Pro Leu Pro Gln Gly Asn
275 280 285
Asp Pro Glu Pro Ser Gly Asp Ser Pro Leu Gly Leu Cys Gln Ser
290 295 300
Glu Cys Met Glu Met Ser Glu Val Phe Asp Asp Ala Ser Asp Gln
305 310 315
Asp Ser Thr Asp Lys Pro Trp Arg Pro Tyr Tyr Asn Tyr Lys Pro
320 325 330
Lys Lys Lys Ser Arg Gln Leu Lys Lys Met Arg Lys Val Asn Trp
335 340 345
Arg Lys Glu His Gly Asn Arg Ser Pro Ser His Lys Cys Lys Tyr
350 355 360
Pro Ala Glu Leu Asp Cys Ala Val Gly Lys Ala Pro Gln Asp Lys
365 370 375
Pro Phe Glu Glu Glu Glu Thr Lys Glu Met Pro Lys Leu Gln Cys
380 385 390
Glu Leu Cys Asp Gly Asp Lys Ala Val Gly Ala Gly Asn Gln Gly
395 400 405
Arg Pro His Arg His Leu Thr Ser Arg Pro Tyr Ala Cys Glu Leu
410 415 420
Cys Ala Lys Gln Phe Gln Ser Pro Ser Thr Leu Lys Met His Met
425 430 435
Arg Cys His Thr Gly Glu Lys Pro Tyr Gln Cys Lys Thr Cys Gly
440 445 450
Arg Cys Phe Ser Val Gln Gly Asn Leu Gln Lys His Glu Arg Ile
455 460 465
His Leu Gly Leu Lys Glu Phe Val Cys Gln Tyr Cys Asn Lys Ala
470 475 480
Phe Thr Leu Asn Glu Thr Leu Lys Ile His Glu Arg Ile His Thr
485 490 495
Gly Glu Lys Arg Tyr His Cys Gln Phe Cys Phe Gln Arg Phe Leu
500 505 510
Tyr Leu Ser Thr Lys Arg Asn His Glu Gln Arg His Ile Arg Glu
515 520 525
His Asn Gly Lys Gly Tyr Ala Cys Phe Gln Cys Pro Lys Ile Cys
530 535 540
Lys Thr Ala Ala Ala Leu Gly Met His Gln Lys Lys His Leu Phe
545 550 555
Lys Ser Pro Ser Gln Gln Glu Lys Ile Gly Asp Val Cys His Glu
560 565 570
Asn Ser Asn Pro Leu Glu Asn Gln His Phe Ile Gly Ser Glu Asp
575 580 585
Asn Asp Gln Lys Asp Asn Ile Gln Thr Gly Val Glu Asn Val Val
590 595 600
Leu

<210> 34
<211> 834
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1576862CD1

<400> 34
Met Glu Glu Lys Arg Arg Lys Tyr Ser Ile Ser Ser Asp Asn Ser
1 5 10 15
Asp Thr Thr Asp Ser His Ala Thr Ser Thr Ser Ala Ser Arg Cys
20 25 30
Ser Lys Leu Pro Ser Ser Thr Lys Ser Gly Trp Pro Arg Gln Asn
35 40 45
Glu Lys Lys Pro Ser Glu Val Phe Arg Thr Asp Leu Ile Thr Ala
50 55 60
Met Lys Ile Pro Asp Ser Tyr Gln Leu Ser Pro Asp Asp Tyr Tyr
65 70 75
Ile Leu Ala Asp Pro Trp Arg Gln Glu Trp Glu Lys Gly Val Gln
80 85 90
Val Pro Ala Gly Ala Glu Ala Ile Pro Glu Pro Val Val Arg Ile
95 100 105
Leu Pro Pro Leu Glu Gly Pro Pro Ala Gln Ala Ser Pro Ser Ser
110 115 120
Thr Met Leu Gly Glu Gly Ser Gln Pro Asp Trp Pro Gly Gly Ser
125 130 135
Arg Tyr Asp Leu Asp Glu Ile Asp Ala Tyr Trp Leu Glu Leu Ile
140 145 150
Asn Ser Glu Leu Lys Glu Met Glu Arg Pro Glu Leu Asp Glu Leu
155 160 165
Thr Leu Glu Arg Val Leu Glu Glu Leu Glu Thr Leu Cys His Gln
170 175 180
Asn Met Ala Arg Ala Ile Glu Thr Gln Glu Gly Leu Gly Ile Glu
185 190 195
Tyr Asp Glu Asp Val Val Cys Asp Val Cys Arg Ser Pro Glu Gly
200 205 210
Glu Asp Gly Asn Glu Met Val Phe Cys Asp Lys Cys Asn Val Cys
215 220 225
Val His Gln Ala Cys Tyr Gly Ile Leu Lys Val Pro Thr Gly Ser
230 235 240
Trp Leu Cys Arg Thr Cys Ala Leu Gly Val Gln Pro Lys Cys Leu
245 250 255
Leu Cys Pro Lys Arg Gly Gly Ala Leu Lys Pro Thr Arg Ser Gly
260 265 270
Thr Lys Trp Val His Val Ser Cys Ala Leu Trp Ile Pro Glu Val
275 280 285
Ser Ile Gly Cys Pro Glu Lys Met Glu Pro Ile Thr Lys Ile Ser
290 295 300
His Ile Pro Ala Ser Arg Trp Ala Leu Ser Cys Ser Leu Cys Lys
305 310 315
Glu Cys Thr Gly Thr Cys Ile Gln Cys Ser Met Pro Ser Cys Val
320 325 330
Thr Ala Phe His Val Thr Cys Ala Phe Asp His Gly Leu Glu Met
335 340 345
Arg Thr Ile Leu Ala Asp Asn Asp Glu Val Lys Phe Lys Ser Phe
350 355 360
Cys Gln Glu His Ser Asp Gly Gly Pro Arg Asn Glu Pro Thr Ser
365 370 375
Glu Pro Thr Glu Pro Ser Gln Ala Gly Glu Asp Leu Glu Lys Val
380 385 390
Thr Leu Arg Lys Gln Arg Leu Gln Gln Leu Glu Glu Asp Phe Tyr

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                395                 400                 405
Glu Leu Val Glu Pro Ala Glu Val Ala Glu Arg Leu Asp Leu Ala
                410                 415                 420
Glu Ala Leu Val Asp Phe Ile Tyr Gln Tyr Trp Lys Leu Lys Arg
                425                 430                 435
Lys Ala Asn Ala Asn Gln Pro Leu Leu Thr Pro Lys Thr Asp Glu
                440                 445                 450
Val Asp Asn Leu Ala Gln Gln Glu Gln Asp Val Leu Tyr Arg Arg
                455                 460                 465
Leu Lys Leu Phe Thr His Leu Arg Gln Asp Leu Glu Arg Val Arg
                470                 475                 480
Asn Leu Cys Tyr Met Val Thr Arg Arg Glu Arg Thr Lys His Ala
                485                 490                 495
Ile Cys Lys Leu Gln Glu Gln Ile Phe His Leu Gln Met Lys Leu
                500                 505                 510
Ile Glu Gln Asp Leu Cys Arg Glu Arg Ser Gly Arg Arg Ala Lys
                515                 520                 525
Gly Lys Lys Ser Asp Ser Lys Arg Lys Gly Cys Glu Gly Ser Lys
                530                 535                 540
Gly Ser Thr Glu Lys Lys Glu Lys Val Lys Ala Gly Pro Asp Ser
                545                 550                 555
Val Leu Gly Gln Leu Ala Gly Leu Ser Thr Ser Phe Pro Ile Asp
                560                 565                 570
Gly Thr Phe Phe Asn Ser Trp Leu Ala Gln Ser Val Gln Ile Thr
                575                 580                 585
Ala Glu Asn Met Ala Met Ser Glu Trp Pro Leu Asn Asn Gly His
                590                 595                 600
Arg Glu Asp Pro Ala Pro Gly Leu Leu Ser Glu Glu Leu Leu Gln
                605                 610                 615
Asp Glu Glu Thr Leu Leu Ser Phe Met Arg Asp Pro Ser Leu Arg
                620                 625                 630
Pro Gly Asp Pro Ala Arg Lys Ala Arg Gly Arg Thr Arg Leu Pro
                635                 640                 645
Ala Lys Lys Lys Pro Pro Pro Pro Pro Pro Gln Asp Gly Pro Gly
                650                 655                 660
Ser Arg Thr Thr Pro Asp Lys Ala Pro Lys Lys Thr Trp Gly Gln
                665                 670                 675
Asp Ala Gly Ser Gly Lys Gly Gly Gln Gly Pro Pro Thr Arg Lys
                680                 685                 690
Pro Pro Arg Arg Thr Ser Ser His Leu Pro Ser Ser Pro Ala Ala
                695                 700                 705
Gly Asp Cys Pro Ile Leu Ala Thr Pro Glu Ser Pro Pro Pro Leu
                710                 715                 720
Ala Pro Glu Thr Pro Asp Glu Ala Ala Ser Val Ala Ala Asp Ser
                725                 730                 735
Asp Val Gln Val Pro Gly Pro Ala Ala Ser Pro Lys Pro Leu Gly
                740                 745                 750
Arg Leu Arg Pro Pro Arg Glu Ser Lys Val Thr Arg Arg Leu Pro
                755                 760                 765
Gly Ala Arg Pro Asp Ala Gly Met Gly Pro Pro Ser Ala Val Ala
                770                 775                 780
Glu Arg Pro Lys Val Ser Leu His Phe Asp Thr Glu Thr Asp Gly
                785                 790                 795
Tyr Phe Ser Asp Gly Glu Met Ser Asp Ser Asp Val Glu Ala Glu
                800                 805                 810
Asp Gly Gly Val Gln Arg Gly Pro Arg Glu Ala Gly Ala Glu Glu
                815                 820                 825
Val Val Arg Met Gly Val Leu Ala Ser
                830
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<210> 35
<211> 499
<212> PRT

<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1609731CD1

<400> 35
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Met Ala Gln Gly Leu Val Thr Phe Arg Asp Val Ala Ile Glu Phe
 1               5                  10                  15
Ser Leu Glu Glu Trp Lys Cys Leu Glu Pro Ala Gln Arg Asp Leu
                20                  25                  30
Tyr Arg Glu Val Thr Leu Glu Asn Phe Gly His Leu Ala Ser Leu
                35                  40                  45
Gly Leu Ser Ile Ser Lys Pro Asp Val Val Ser Leu Leu Glu Gln
                50                  55                  60
Gly Lys Glu Pro Trp Met Ile Ala Asn Asp Val Thr Gly Pro Trp
                65                  70                  75
Cys Pro Asp Leu Glu Ser Arg Cys Glu Lys Phe Leu Gln Lys Asp
                80                  85                  90
Ile Phe Glu Ile Gly Ala Phe Asn Trp Glu Ile Met Glu Ser Leu
                95                 100                 105
Lys Cys Ser Asp Leu Glu Gly Ser Asp Phe Arg Ala Asp Trp Glu
               110                 115                 120
Cys Glu Gly Gln Phe Glu Arg Gln Val Asn Glu Glu Cys Tyr Phe
               125                 130                 135
Lys Gln Val Asn Val Thr Tyr Gly His Met Pro Val Phe Gln His
               140                 145                 150
His Thr Ser His Thr Val Arg Gln Ser Arg Glu Thr Gly Glu Lys
               155                 160                 165
Leu Met Glu Cys His Glu Cys Gly Lys Ala Phe Ser Arg Gly Ser
               170                 175                 180
His Leu Ile Gln His Gln Lys Thr His Thr Gly Glu Lys Pro Phe
               185                 190                 195
Gly Cys Lys Glu Cys Gly Lys Ala Phe Ser Arg Ala Ser His Leu
               200                 205                 210
Val Gln His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Asp Cys
               215                 220                 225
Lys Asp Cys Gly Lys Ala Phe Gly Arg Thr Ser Glu Leu Ile Leu
               230                 235                 240
His Gln Arg Leu His Thr Gly Val Lys Pro Tyr Glu Cys Lys Glu
               245                 250                 255
Cys Gly Lys Thr Phe Arg Gln His Ser Gln Leu Ile Leu His Gln
               260                 265                 270
Arg Thr His Thr Gly Glu Lys Pro Tyr Val Cys Lys Asp Cys Gly
               275                 280                 285
Lys Ala Phe Ile Arg Gly Ser Gln Leu Thr Val His Arg Arg Ile
               290                 295                 300
His Thr Gly Ala Arg Pro Tyr Glu Cys Lys Glu Cys Gly Lys Ala
               305                 310                 315
Phe Arg Gln His Ser Gln Leu Thr Val His Gln Arg Ile His Thr
               320                 325                 330
Gly Glu Lys Pro Tyr Glu Cys Lys Glu Cys Gly Lys Gly Phe Ile
               335                 340                 345
His Ser Ser Glu Val Thr Arg His Gln Arg Asn Ser Phe Trp Gly
               350                 355                 360
Glu Pro Tyr Glu Cys Lys Glu Cys Gly Lys Ala Phe Arg Gln His
               365                 370                 375
Ala Gln Leu Thr Arg His Gln Arg Val His Thr Gly Asp Arg Pro
               380                 385                 390
Tyr Glu Cys Lys Asp Cys Gly Lys Ala Phe Ser Arg Ser Ser Tyr
               395                 400                 405
Leu Ile Gln His Gln Arg Ile His Thr Gly Asp Lys Pro Tyr Glu
               410                 415                 420
```

Cys Lys Glu Cys Gly Lys Ala Phe Ile Arg Val Ser Gln Leu Thr
425 430 435
His His Gln Arg Ile His Thr Cys Glu Lys Pro Tyr Glu Cys Arg
440 445 450
Glu Cys Gly Met Ala Phe Ile Arg Ser Ser Gln Leu Thr Glu His
455 460 465
Gln Arg Ile His Pro Gly Ile Lys Pro Tyr Glu Cys Arg Glu Cys
470 475 480
Gly Gln Ala Phe Ile Leu Gly Ser Gln Leu Ile Glu His Tyr Arg
485 490 495
Ile His Thr Gly

<210> 36
<211> 402
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1674538CD1

<400> 36
Met Tyr Thr Ser Glu Glu Lys Cys Asn Gln Arg Thr Gln Lys Arg
1 5 10 15
Lys Ile Tyr Asn Val Cys Pro Arg Lys Gly Lys Lys Ile Phe Ile
20 25 30
His Met His Glu Ile Ile Gln Ile Asp Gly His Ile Tyr Gln Cys
35 40 45
Leu Glu Cys Lys Gln Asn Phe Cys Glu Asn Leu Ala Leu Ile Met
50 55 60
Cys Glu Arg Thr His Thr Gly Glu Lys Pro Tyr Lys Cys Asp Met
65 70 75
Cys Glu Lys Thr Phe Val Gln Ser Ser Asp Leu Thr Ser His Gln
80 85 90
Arg Ile His Asn Tyr Glu Lys Pro Tyr Lys Cys Ser Lys Cys Glu
95 100 105
Lys Ser Phe Trp His His Leu Ala Leu Ser Gly His Gln Arg Thr
110 115 120
His Ala Gly Lys Lys Phe Tyr Thr Cys Asp Ile Cys Gly Lys Asn
125 130 135
Phe Gly Gln Ser Ser Asp Leu Leu Val His Gln Arg Ser His Thr
140 145 150
Gly Glu Lys Pro Tyr Leu Cys Ser Glu Cys Asp Lys Cys Phe Ser
155 160 165
Arg Ser Thr Asn Leu Ile Arg His Arg Arg Thr His Thr Gly Glu
170 175 180
Lys Pro Phe Lys Cys Leu Glu Cys Glu Lys Ala Phe Ser Gly Lys
185 190 195
Ser Asp Leu Ile Ser His Gln Arg Thr His Thr Gly Glu Arg Pro
200 205 210
Tyr Lys Cys Asn Lys Cys Glu Lys Ser Tyr Arg His Arg Ser Ala
215 220 225
Phe Ile Val His Lys Arg Val His Thr Gly Glu Lys Pro Tyr Lys
230 235 240
Cys Gly Ala Cys Glu Lys Cys Phe Gly Gln Lys Ser Asp Leu Ile
245 250 255
Val His Gln Arg Val His Thr Gly Glu Lys Pro Tyr Lys Cys Leu
260 265 270
Glu Cys Met Arg Ser Phe Thr Arg Ser Ala Asn Leu Ile Arg His
275 280 285
Gln Ala Thr His Thr His Thr Phe Lys Cys Leu Glu Tyr Glu Lys
290 295 300

Ser Phe Asn Cys Ser Ser Asp Leu Ile Val His Gln Arg Ile His
305 310 315
Met Glu Glu Lys Pro His Gln Trp Ser Ala Cys Glu Ser Gly Phe
320 325 330
Leu Leu Gly Met Asp Phe Val Ala Gln Gln Lys Met Arg Thr Gln
335 340 345
Thr Glu Glu Leu His Tyr Lys Tyr Thr Val Cys Asp Lys Ser Phe
350 355 360
His Gln Ser Ser Ala Leu Leu Gln His Gln Thr Val His Ile Gly
365 370 375
Glu Lys Pro Phe Val Cys Asn Val Ser Glu Lys Gly Leu Glu Leu
380 385 390
Ser Pro Pro His Ala Ser Glu Ala Ser Gln Met Ser
395 400

<210> 37
<211> 579
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1675287CD1

<400> 37
Met Ile Arg Glu Gly Glu Ala Ala Gly Ala Cys Pro Glu Glu Ile
1 5 10 15
Phe Ser Ala Leu Gln Tyr Ser Gly Thr Glu Val Pro Leu Gln Trp
20 25 30
Leu Arg Ser Glu Leu Pro Tyr Val Leu Glu Met Val Ala Glu Leu
35 40 45
Ala Gly Gln Gln Asp Pro Gly Leu Gly Ala Phe Ser Cys Gln Glu
50 55 60
Ala Arg Arg Ala Trp Leu Asp Arg His Gly Asn Leu Asp Glu Ala
65 70 75
Val Glu Glu Cys Val Arg Thr Arg Arg Arg Lys Val Gln Glu Leu
80 85 90
Gln Ser Leu Gly Phe Gly Pro Glu Glu Gly Ser Leu Gln Ala Leu
95 100 105
Phe Gln His Gly Gly Asp Val Ser Arg Ala Leu Thr Glu Leu Gln
110 115 120
Arg Gln Arg Leu Glu Pro Phe Arg Gln Arg Leu Trp Asp Ser Gly
125 130 135
Pro Glu Pro Thr Pro Ser Trp Asp Gly Pro Asp Lys Gln Ser Leu
140 145 150
Val Arg Arg Leu Leu Ala Val Tyr Ala Leu Pro Ser Trp Gly Arg
155 160 165
Ala Glu Leu Ala Leu Ser Leu Leu Gln Glu Thr Pro Arg Asn Tyr
170 175 180
Glu Leu Gly Asp Val Val Glu Ala Val Arg His Ser Gln Asp Arg
185 190 195
Ala Phe Leu Arg Arg Leu Leu Ala Gln Glu Cys Ala Val Cys Gly
200 205 210
Trp Ala Leu Pro His Asn Arg Met Gln Ala Leu Thr Ser Cys Glu
215 220 225
Cys Thr Ile Cys Pro Asp Cys Phe Arg Gln His Phe Thr Ile Ala
230 235 240
Leu Lys Glu Lys His Ile Thr Asp Met Val Cys Pro Ala Cys Gly
245 250 255
Arg Pro Asp Leu Thr Asp Asp Thr Gln Leu Leu Ser Tyr Phe Ser
260 265 270
Thr Leu Asp Ile Gln Leu Arg Glu Ser Leu Glu Pro Asp Ala Tyr
275 280 285

Ala Leu Phe His Lys Lys Leu Thr Glu Gly Val Leu Met Arg Asp
290 295 300
Pro Lys Phe Leu Trp Cys Ala Gln Cys Ser Phe Gly Phe Ile Tyr
305 310 315
Glu Arg Glu Gln Leu Glu Ala Thr Cys Pro Gln Cys His Gln Thr
320 325 330
Phe Cys Val Arg Cys Lys Arg Gln Trp Glu Glu Gln His Arg Gly
335 340 345
Arg Ser Cys Glu Asp Phe Gln Asn Trp Lys Arg Met Asn Asp Pro
350 355 360
Glu Tyr Gln Ala Gln Gly Leu Ala Met Tyr Leu Gln Glu Asn Gly
365 370 375
Ile Asp Cys Pro Lys Cys Lys Phe Ser Tyr Ala Leu Ala Arg Gly
380 385 390
Gly Cys Met His Phe His Cys Thr Gln Cys Arg His Gln Phe Cys
395 400 405
Ser Gly Cys Tyr Asn Ala Phe Tyr Ala Lys Asn Lys Cys Pro Glu
410 415 420
Pro Asn Cys Arg Val Lys Lys Ser Leu His Gly His His Pro Arg
425 430 435
Asp Cys Leu Phe Tyr Leu Arg Asp Trp Thr Ala Leu Arg Leu Gln
440 445 450
Lys Leu Leu Gln Asp Asn Asn Val Met Phe Asn Thr Glu Pro Pro
455 460 465
Ala Gly Ala Arg Ala Val Pro Gly Gly Gly Cys Arg Val Ile Glu
470 475 480
Gln Lys Glu Val Pro Asn Gly Leu Arg Asp Glu Ala Cys Gly Lys
485 490 495
Glu Thr Pro Ala Gly Tyr Ala Gly Leu Cys Gln Ala His Tyr Lys
500 505 510
Glu Tyr Leu Val Ser Leu Ile Asn Ala His Ser Leu Asp Pro Ala
515 520 525
Thr Leu Tyr Glu Val Glu Glu Leu Glu Thr Ala Thr Glu Arg Tyr
530 535 540
Leu His Val Arg Pro Gln Pro Leu Ala Gly Glu Asp Pro Pro Ala
545 550 555
Tyr Gln Ala Arg Leu Leu Gln Lys Leu Thr Glu Glu Val Pro Leu
560 565 570
Gly Gln Ser Ile Pro Arg Arg Arg Lys
575

<210> 38
<211> 426
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1693903CD1

<400> 38
Met Pro Pro Lys Lys Gln Ala Gln Ala Gly Gly Ser Lys Lys Ala
1 5 10 15
Glu Gln Lys Lys Lys Glu Lys Ile Ile Glu Asp Lys Thr Phe Gly
20 25 30
Leu Lys Asn Lys Lys Gly Ala Lys Gln Gln Lys Phe Ile Lys Ala
35 40 45
Val Thr His Gln Val Lys Phe Gly Gln Gln Asn Pro Arg Gln Val
50 55 60
Ala Gln Ser Glu Ala Glu Lys Lys Leu Lys Lys Asp Asp Lys Lys
65 70 75
Lys Glu Leu Gln Glu Leu Asn Glu Leu Phe Lys Pro Val Val Ala
80 85 90

Ala Gln Lys Ile Ser Lys Gly Ala Asp Pro Lys Ser Val Val Cys
95 100 105
Ala Phe Phe Lys Gln Gly Gln Cys Thr Lys Gly Asp Lys Cys Lys
110 115 120
Phe Ser His Asp Leu Thr Leu Glu Arg Lys Cys Glu Lys Arg Ser
125 130 135
Val Tyr Ile Asp Ala Arg Asp Glu Glu Leu Glu Lys Asp Thr Met
140 145 150
Asp Asn Trp Asp Glu Lys Lys Leu Glu Glu Val Val Asn Lys Lys
155 160 165
His Gly Glu Ala Glu Lys Lys Lys Pro Lys Thr Gln Ile Val Cys
170 175 180
Lys His Phe Leu Glu Ala Ile Glu Asn Asn Lys Tyr Gly Trp Phe
185 190 195
Trp Val Cys Pro Gly Gly Gly Asp Ile Cys Met Tyr Arg His Ala
200 205 210
Leu Pro Pro Gly Phe Val Leu Lys Lys Asp Lys Lys Lys Glu Glu
215 220 225
Lys Glu Asp Glu Ile Ser Leu Glu Asp Leu Ile Glu Arg Glu Arg
230 235 240
Ser Ala Leu Gly Pro Asn Val Thr Lys Ile Thr Leu Glu Ser Phe
245 250 255
Leu Ala Trp Lys Lys Arg Lys Arg Gln Glu Lys Ile Asp Lys Leu
260 265 270
Glu Gln Asp Met Glu Arg Arg Lys Ala Asp Phe Lys Ala Gly Lys
275 280 285
Ala Leu Val Ile Ser Gly Arg Glu Val Phe Glu Phe Arg Pro Glu
290 295 300
Leu Val Asn Asp Asp Asp Glu Glu Ala Asp Asp Thr Arg Tyr Thr
305 310 315
Gln Gly Thr Gly Gly Asp Glu Val Asp Asp Ser Val Ser Val Asn
320 325 330
Asp Ile Asp Leu Ser Leu Tyr Ile Pro Arg Asp Val Asp Glu Thr
335 340 345
Gly Ile Thr Val Ala Ser Leu Glu Arg Phe Ser Thr Tyr Thr Ser
350 355 360
Asp Lys Asp Glu Asn Lys Leu Ser Glu Ala Ser Gly Gly Arg Ala
365 370 375
Glu Asn Gly Glu Arg Ser Asp Leu Glu Glu Asp Asn Glu Arg Glu
380 385 390
Gly Thr Glu Asn Gly Ala Ile Asp Ala Val Pro Val Asp Glu Asn
395 400 405
Leu Phe Thr Gly Glu Asp Leu Asp Glu Leu Glu Glu Glu Leu Asn
410 415 420
Thr Leu Asp Leu Glu Glu
425

<210> 39
<211> 266
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1702962CD1

<400> 39
Met Gly Ser Lys Thr Leu Pro Ala Pro Val Pro Ile His Pro Ser
1 5 10 15
Leu Gln Leu Thr Asn Tyr Ser Phe Leu Gln Ala Val Asn Gly Leu
20 25 30
Pro Thr Val Pro Ser Asp His Leu Pro Asn Leu Tyr Gly Phe Ser
35 40 45

```
Ala Leu His Ala Val His Leu His Gln Trp Thr Leu Gly Tyr Pro
                50                  55                  60
Ala Met His Leu Pro Arg Ser Ser Phe Ser Lys Val Pro Gly Thr
                65                  70                  75
Val Ser Ser Leu Val Asp Ala Arg Phe Gln Leu Pro Ala Phe Pro
                80                  85                  90
Trp Phe Pro His Val Ile Gln Pro Lys Pro Glu Ile Thr Ala Gly
                95                  100                 105
Gly Ser Val Pro Ala Leu Lys Thr Lys Pro Arg Phe Asp Phe Ala
                110                 115                 120
Asn Leu Ala Leu Ala Ala Thr Gln Glu Asp Pro Ala Lys Leu Gly
                125                 130                 135
Arg Arg Glu Gly Pro Gly Ser Pro Ala Gly Gly Leu Gly Ala Leu
                140                 145                 150
Leu Asp Val Thr Lys Leu Ser Pro Glu Lys Lys Pro Thr Arg Gly
                155                 160                 165
Arg Leu Pro Ser Lys Thr Lys Lys Glu Phe Val Cys Lys Phe Cys
                170                 175                 180
Gly Arg Gln Phe Thr Lys Ser Tyr Asn Leu Leu Ile His Glu Arg
                185                 190                 195
Thr His Thr Asp Glu Arg Pro Tyr Thr Cys Asp Ile Cys His Lys
                200                 205                 210
Ala Phe Arg Arg Gln Asp His Leu Arg Asp His Arg Tyr Ile His
                215                 220                 225
Ser Lys Glu Lys Pro Phe Lys Cys Gln Glu Cys Gly Lys Gly Phe
                230                 235                 240
Cys Gln Ser Arg Thr Leu Ala Val His Lys Thr Leu His Ser Gln
                245                 250                 255
Val Lys Glu Leu Lys Thr Ser Lys Ile Lys Cys
                260                 265

<210> 40
<211> 358
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1712916CD1

<400> 40
Met Asn Thr Ile Val Phe Asn Lys Leu Ser Gly Ala Val Leu Phe
  1               5                   10                  15
Glu Asp Gly Gly Ala Ser Glu Arg Glu Arg Gly Gly Arg Pro Tyr
                20                  25                  30
Ser Gly Val Leu Asp Ser Pro His Ala Arg Pro Glu Val Gly Ile
                35                  40                  45
Pro Asp Gly Pro Pro Leu Lys Asp Asn Leu Gly Leu Arg His Arg
                50                  55                  60
Arg Thr Gly Ala Arg Gln Asn Gly Gly Lys Val Arg His Lys Arg
                65                  70                  75
Gln Ala Leu Gln Asp Met Ala Arg Pro Leu Lys Gln Trp Leu Tyr
                80                  85                  90
Lys His Arg Asp Asn Pro Tyr Pro Thr Lys Thr Glu Lys Ile Leu
                95                  100                 105
Leu Ala Leu Gly Ser Gln Met Thr Leu Val Gln Val Ser Asn Trp
                110                 115                 120
Phe Ala Asn Ala Arg Arg Arg Leu Lys Asn Thr Val Arg Gln Pro
                125                 130                 135
Asp Leu Ser Trp Ala Leu Arg Ile Lys Leu Tyr Asn Lys Tyr Val
                140                 145                 150
Gln Gly Asn Ala Glu Arg Leu Ser Val Ser Ser Asp Asp Ser Cys
                155                 160                 165
```

Ser Glu Asp Gly Glu Asn Pro Pro Arg Thr His Met Asn Glu Gly
170 175 180
Gly Tyr Asn Thr Pro Val His His Pro Val Ile Lys Ser Glu Asn
185 190 195
Ser Val Ile Lys Ala Gly Val Arg Pro Glu Ser Arg Ala Ser Glu
200 205 210
Asp Tyr Val Ala Pro Pro Lys Tyr Lys Ser Ser Leu Leu Asn Arg
215 220 225
Tyr Leu Asn Asp Ser Leu Arg His Val Met Ala Thr Asn Thr Thr
230 235 240
Met Met Gly Lys Thr Arg Gln Arg Asn His Ser Gly Ser Phe Ser
245 250 255
Ser Asn Glu Phe Glu Glu Glu Leu Val Ser Pro Ser Ser Ser Glu
260 265 270
Thr Glu Gly Asn Phe Val Tyr Arg Thr Asp Thr Leu Glu Asn Gly
275 280 285
Ser Asn Lys Gly Glu Ser Ala Arg Asn Arg Lys Gly Pro Ser Lys
290 295 300
Asp Asp Thr Tyr Trp Lys Glu Ile Asn Ala Ala Met Ala Leu Thr
305 310 315
Asn Leu Ala Gln Gly Lys Asp Lys Leu Gln Gly Thr Thr Ser Cys
320 325 330
Ile Ile Gln Lys Ser Ser His Ile Ala Gly Val Arg Leu Ser Ser
335 340 345
Ala Val Val His Ser Leu Arg Ala Cys Ala Phe Ser Gln
350 355

<210> 41
<211> 260
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1748313CD1

<400> 41
Met Met Asp Pro Cys Ser Val Gly Val Gln Leu Arg Thr Thr Asn
1 5 10 15
Glu Cys His Lys Thr Tyr Tyr Thr Arg His Thr Gly Phe Lys Thr
20 25 30
Leu Gln Glu Leu Ser Ser Asn Asp Met Leu Leu Leu Gln Leu Arg
35 40 45
Thr Gly Met Thr Leu Ser Gly Asn Asn Thr Ile Cys Phe His His
50 55 60
Val Lys Ile Tyr Ile Asp Arg Phe Glu Asp Leu Gln Lys Ser Cys
65 70 75
Cys Asp Pro Phe Asn Ile His Lys Lys Leu Ala Lys Lys Asn Leu
80 85 90
His Val Ile Asp Leu Asp Asp Ala Thr Phe Leu Ser Ala Lys Phe
95 100 105
Gly Arg Gln Leu Val Pro Gly Trp Lys Leu Cys Pro Lys Cys Thr
110 115 120
Gln Ile Ile Asn Gly Ser Val Asp Val Asp Thr Glu Asp Arg Gln
125 130 135
Lys Arg Lys Pro Glu Ser Asp Gly Arg Thr Ala Lys Ala Leu Arg
140 145 150
Ser Leu Gln Phe Thr Asn Pro Gly Arg Gln Thr Glu Phe Ala Pro
155 160 165
Glu Thr Gly Lys Arg Glu Lys Arg Arg Leu Thr Lys Asn Ala Thr
170 175 180
Ala Gly Ser Asp Arg Gln Val Ile Pro Ala Lys Ser Lys Val Tyr
185 190 195

```
Asp Ser Gln Gly Leu Leu Ile Phe Ser Gly Met Asp Leu Cys Asp
                200                 205                 210
Cys Leu Asp Glu Asp Cys Leu Gly Cys Phe Tyr Ala Cys Pro Ala
                215                 220                 225
Cys Gly Ser Thr Lys Cys Gly Ala Glu Cys Arg Cys Asp Arg Lys
                230                 235                 240
Trp Leu Tyr Glu Gln Ile Glu Ile Glu Gly Gly Glu Ile Ile His
                245                 250                 255
Asn Lys His Ala Gly
                260
```

<210> 42
<211> 263
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1754833CD1

<400> 42

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Met Val Leu Pro Pro Pro Gln Leu Pro Gln Thr Arg Ala Gly His
 1               5                  10                  15
Arg Trp Ser Thr Trp Thr Ser Thr Cys Ser Arg Cys Arg Arg Ala
                20                  25                  30
Thr Asp Ser Leu Leu Ser Ala Ser Ser Met Thr Ala Ser Arg Ser
                35                  40                  45
Pro Arg Ser Leu Leu Gly Arg Arg Leu Thr Thr Ala Gly Thr Leu
                50                  55                  60
Arg Ala Gly Gly Arg Glu Thr Ile Arg Pro Gly Thr Gly Thr Ala
                65                  70                  75
Pro Asp Ser Pro Ala Pro Ala Ser Pro Arg Gly Gly Pro Pro Ala
                80                  85                  90
Gly Thr Lys Ala Ser Pro Arg Trp Lys Gly Ser Ser Ser Ser Ser
                95                 100                 105
Ser Thr Ala Ser Ser Arg Pro Pro Pro Ser Pro Ala Trp Ala Pro
                110                 115                 120
Trp Gly Val Leu His Ser Asn Pro Met Asp Tyr Ala Trp Gly Ala
                125                 130                 135
Asn Gly Leu Asp Ala Ile Ile Thr Gln Leu Leu Asn Gln Phe Glu
                140                 145                 150
Asn Thr Gly Pro Pro Pro Ala Asp Lys Glu Lys Ile Gln Ala Leu
                155                 160                 165
Pro Thr Val Pro Val Thr Glu Glu His Val Gly Ser Gly Leu Glu
                170                 175                 180
Cys Pro Val Cys Lys Asp Asp Tyr Ala Leu Gly Glu Arg Val Arg
                185                 190                 195
Gln Leu Pro Cys Asn His Leu Phe His Asp Gly Cys Ile Val Pro
                200                 205                 210
Trp Leu Glu Gln His Asp Ser Cys Pro Val Cys Arg Lys Ser Leu
                215                 220                 225
Thr Gly Gln Asn Thr Ala Thr Asn Pro Pro Gly Leu Thr Gly Val
                230                 235                 240
Ser Phe Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Pro Ser
                245                 250                 255
Asn Glu Asn Ala Thr Ser Asn Ser
                260
```

<210> 43
<211> 581
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1798701CD1

<400> 43
Met Asp Glu Asp Tyr Tyr Gly Ser Ala Ala Glu Trp Gly Asp Glu
1 5 10 15
Ala Asp Gly Gly Gln Gln Glu Asp Asp Ser Gly Glu Gly Glu Asp
20 25 30
Asp Ala Glu Val Gln Gln Glu Cys Leu His Lys Phe Ser Thr Arg
35 40 45
Asp Tyr Ile Met Glu Pro Ser Ile Phe Asn Thr Leu Lys Arg Tyr
50 55 60
Phe Gln Ala Gly Gly Ser Pro Glu Asn Val Ile Gln Leu Leu Ser
65 70 75
Glu Asn Tyr Thr Ala Val Ala Gln Thr Val Asn Leu Leu Ala Glu
80 85 90
Trp Leu Ile Gln Thr Gly Val Glu Pro Val Gln Val Gln Glu Thr
95 100 105
Val Glu Asn Tyr Leu Lys Ser Leu Leu Ile Lys His Phe Asp Pro
110 115 120
Arg Lys Ala Asp Ser Ile Phe Thr Glu Glu Gly Glu Thr Pro Ala
125 130 135
Trp Leu Glu Gln Met Ile Ala His Thr Thr Trp Arg Asp Leu Phe
140 145 150
Tyr Lys Leu Ala Glu Ala His Pro Asp Cys Leu Met Leu Asn Phe
155 160 165
Thr Val Lys Leu Ile Ser Asp Ala Gly Tyr Gln Gly Glu Ile Thr
170 175 180
Ser Val Ser Thr Ala Cys Gln Gln Leu Glu Val Phe Ser Arg Val
185 190 195
Leu Arg Thr Ser Leu Ala Thr Ile Leu Asp Gly Gly Glu Glu Asn
200 205 210
Leu Glu Lys Asn Leu Pro Glu Phe Ala Lys Met Val Cys His Gly
215 220 225
Glu His Thr Tyr Leu Phe Ala Gln Ala Met Met Ser Val Leu Ala
230 235 240
Gln Glu Glu Gln Gly Gly Ser Ala Val Arg Arg Ile Ala Gln Glu
245 250 255
Val Gln Arg Phe Ala Gln Glu Lys Gly His Asp Ala Ser Gln Ile
260 265 270
Thr Leu Ala Leu Gly Thr Ala Ala Ser Tyr Pro Arg Ala Cys Gln
275 280 285
Ala Leu Gly Ala Met Leu Ser Lys Gly Ala Leu Asn Pro Ala Asp
290 295 300
Ile Thr Val Leu Phe Lys Met Phe Thr Ser Met Asp Pro Pro Pro
305 310 315
Val Glu Leu Ile Arg Val Pro Ala Phe Leu Asp Leu Phe Met Gln
320 325 330
Ser Leu Phe Lys Pro Gly Ala Arg Ile Asn Gln Asp His Lys His
335 340 345
Lys Tyr Ile His Ile Leu Ala Tyr Ala Ala Ser Val Val Glu Thr
350 355 360
Trp Lys Lys Asn Lys Arg Val Ser Ile Asn Lys Asp Glu Leu Lys
365 370 375
Ser Thr Ser Lys Ala Val Glu Thr Val His Asn Leu Cys Cys Asn
380 385 390
Glu Asn Lys Gly Ala Ser Glu Leu Val Ala Glu Leu Ser Thr Leu
395 400 405
Tyr Gln Cys Ile Arg Phe Pro Val Val Ala Met Gly Val Leu Lys
410 415 420
Trp Val Asp Trp Thr Val Ser Glu Pro Arg Tyr Phe Gln Leu Gln
425 430 435

Thr Asp His Thr Pro Val His Leu Ala Leu Leu Asp Glu Ile Ser
440 445 450
Thr Cys His Gln Leu Leu His Pro Gln Val Leu Gln Leu Leu Val
455 460 465
Lys Leu Phe Glu Thr Glu His Ser Gln Leu Asp Val Met Glu Gln
470 475 480
Leu Glu Leu Lys Lys Thr Leu Leu Asp Arg Met Val His Leu Leu
485 490 495
Ser Arg Gly Tyr Val Leu Pro Val Val Ser Tyr Ile Arg Lys Cys
500 505 510
Leu Glu Lys Leu Asp Thr Asp Ile Ser Leu Ile Arg Tyr Phe Val
515 520 525
Thr Glu Val Leu Asp Val Ile Ala Pro Pro Tyr Thr Ser Asp Phe
530 535 540
Val Gln Leu Phe Leu Pro Ile Leu Glu Asn Asp Ser Ile Ala Gly
545 550 555
Thr Ile Lys Thr Glu Gly Glu His Asp Pro Val Thr Glu Phe Ile
560 565 570
Ala His Cys Lys Ser Asn Phe Ile Met Val Asn
575 580

<210> 44
<211> 117
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1842496CD1

<400> 44
Met Gln Lys Ser Cys Glu Glu Asn Glu Gly Lys Pro Gln Asn Met
1 5 10 15
Pro Lys Ala Glu Glu Asp Arg Pro Leu Glu Asp Val Pro Gln Glu
20 25 30
Ala Glu Gly Asn Pro Gln Pro Ser Glu Glu Gly Val Ser Gln Glu
35 40 45
Ala Glu Gly Asn Pro Arg Gly Gly Pro Asn Gln Pro Gly Gln Gly
50 55 60
Phe Lys Glu Asp Thr Pro Val Arg His Leu Asp Pro Glu Glu Met
65 70 75
Ile Arg Gly Val Asp Glu Leu Glu Arg Leu Arg Glu Glu Ile Arg
80 85 90
Arg Val Arg Asn Lys Phe Val Met Met His Trp Lys Gln Arg His
95 100 105
Ser Arg Ser Arg Pro Tyr Pro Val Cys Phe Arg Pro
110 115

<210> 45
<211> 202
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1868613CD1

<400> 45
Met Ala Lys Val Ser Val Leu Asn Val Ala Val Leu Glu Asn Pro
1 5 10 15
Ser Pro Phe His Ser Pro Phe Arg Phe Glu Ile Ser Phe Glu Cys
20 25 30
Ser Glu Ala Leu Ala Asp Asp Leu Glu Trp Lys Ile Ile Tyr Val

```
                35                  40                  45
Gly Ser Ala Glu Ser Glu Glu Phe Asp Gln Ile Leu Asp Ser Val
                50                  55                  60
Leu Val Gly Pro Val Pro Ala Gly Arg His Met Phe Val Phe Gln
                65                  70                  75
Ala Asp Ala Pro Asn Pro Ser Leu Ile Pro Glu Thr Asp Ala Val
                80                  85                  90
Gly Val Thr Val Val Leu Ile Thr Cys Thr Tyr His Gly Gln Glu
                95                 100                 105
Phe Ile Arg Val Gly Tyr Tyr Val Asn Asn Glu Tyr Leu Asn Pro
               110                 115                 120
Glu Leu Arg Glu Asn Pro Pro Met Lys Pro Asp Phe Ser Gln Leu
               125                 130                 135
Gln Arg Asn Ile Leu Ala Ser Asn Pro Arg Val Thr Arg Phe His
               140                 145                 150
Ile Asn Trp Asp Asn Asn Met Asp Arg Leu Glu Ala Ile Glu Thr
               155                 160                 165
Gln Asp Pro Ser Leu Gly Cys Gly Leu Pro Leu Asn Cys Thr Pro
               170                 175                 180
Ile Lys Gly Leu Gly Leu Pro Gly Cys Ile Pro Gly Leu Leu Pro
               185                 190                 195
Glu Asn Ser Met Asp Cys Ile
               200

&lt;210&gt; 46
&lt;211&gt; 442
&lt;212&gt; PRT
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; misc_feature
&lt;223&gt; Incyte ID No: 1870609CD1

&lt;400&gt; 46
Met Leu Val Ala Lys Leu Ile Gln Cys Ile Val Phe Gly Pro Leu
  1               5                  10                  15
Arg Val Ser Glu Arg Gln Ser Leu Leu Val Thr Val Arg Thr Ala
                20                  25                  30
His Val Ile Leu Arg Tyr Val Ile His Leu Trp Asp Leu Asn His
                35                  40                  45
Glu Gly Thr Trp Glu Gly Lys Gly Thr Tyr Val Tyr Tyr Thr Asp
                50                  55                  60
Phe Val Met Glu Leu Thr Leu Leu Ser Leu Asp Leu Met His His
                65                  70                  75
Ile His Met Leu Leu Phe Gly Asn Ile Trp Leu Ser Met Ala Ser
                80                  85                  90
Leu Val Ile Phe Met Gln Leu Arg Tyr Leu Phe His Glu Val Gln
                95                 100                 105
Arg Arg Ile Arg Arg His Lys Asn Tyr Leu Arg Val Val Gly Asn
               110                 115                 120
Met Glu Ala Arg Phe Ala Val Ala Thr Pro Glu Glu Leu Ala Val
               125                 130                 135
Asn Asn Asp Asp Cys Ala Ile Cys Trp Asp Ser Met Gln Ala Ala
               140                 145                 150
Arg Lys Leu Pro Cys Gly His Leu Phe His Asn Ser Cys Leu Arg
               155                 160                 165
Ser Trp Leu Glu Gln Asp Thr Ser Cys Pro Thr Cys Arg Met Ser
               170                 175                 180
Leu Asn Ile Ala Asp Asn Asn Arg Val Arg Glu Glu His Gln Gly
               185                 190                 195
Glu Asn Leu Asp Glu Asn Leu Val Pro Val Ala Ala Ala Glu Gly
               200                 205                 210
Arg Pro Arg Leu Asn Gln His Asn His Phe Phe His Phe Asp Gly
```

```
                215                 220                 225
Ser Arg Ile Ala Ser Trp Leu Pro Ser Phe Ser Val Glu Val Met
                230                 235                 240
His Thr Thr Asn Ile Leu Gly Ile Thr Gln Ala Ser Asn Ser Gln
                245                 250                 255
Leu Asn Ala Met Ala His Gln Ile Gln Glu Met Phe Pro Gln Val
                260                 265                 270
Pro Tyr His Leu Val Leu Gln Asp Leu Gln Leu Thr Arg Ser Val
                275                 280                 285
Glu Ile Thr Thr Asp Asn Ile Leu Glu Gly Arg Ile Gln Val Pro
                290                 295                 300
Phe Pro Thr Gln Arg Ser Asp Ser Ile Arg Pro Ala Leu Asn Ser
                305                 310                 315
Pro Val Glu Arg Pro Ser Ser Asp Gln Glu Glu Gly Glu Thr Ser
                320                 325                 330
Ala Gln Thr Glu Arg Val Pro Leu Asp Leu Ser Pro Arg Leu Glu
                335                 340                 345
Glu Thr Leu Asp Phe Gly Glu Val Glu Val Glu Pro Ser Glu Val
                350                 355                 360
Glu Asp Phe Glu Ala Arg Gly Ser Arg Phe Ser Lys Ser Ala Asp
                365                 370                 375
Glu Arg Gln Arg Met Leu Val Gln Arg Lys Asp Glu Leu Leu Gln
                380                 385                 390
Gln Ala Arg Lys Arg Phe Leu Asn Lys Ser Ser Glu Asp Asp Ala
                395                 400                 405
Ala Ser Glu Ser Phe Leu Pro Ser Glu Gly Ala Ser Ser Asp Pro
                410                 415                 420
Val Thr Leu Arg Arg Arg Met Leu Ala Ala Ala Ala Glu Arg Arg
                425                 430                 435
Leu Gln Lys Gln Gln Thr Ser
                440

<210> 47
<211> 765
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1871961CD1

<400> 47
Met Phe Ser Gln Gln Gln Gln Gln Gln Leu Gln Gln Gln Gln Gln
 1               5                  10                  15
Gln Leu Gln Gln Leu Gln Gln Gln Gln Leu Gln Gln Gln Gln Leu
                20                  25                  30
Gln Gln Gln Gln Leu Leu Gln Leu Gln Gln Leu Leu Gln Gln Ser
                35                  40                  45
Pro Pro Gln Ala Pro Leu Pro Met Ala Val Ser Arg Gly Leu Pro
                50                  55                  60
Pro Gln Gln Pro Gln Gln Pro Leu Leu Asn Leu Gln Gly Thr Asn
                65                  70                  75
Ser Ala Ser Leu Leu Asn Gly Ser Met Leu Gln Arg Ala Leu Leu
                80                  85                  90
Leu Gln Gln Leu Gln Gly Leu Asp Gln Phe Ala Met Pro Pro Ala
                95                  100                 105
Thr Tyr Asp Thr Ala Gly Leu Thr Met Pro Thr Ala Thr Leu Gly
                110                 115                 120
Asn Leu Arg Gly Tyr Gly Met Ala Ser Pro Gly Leu Ala Ala Pro
                125                 130                 135
Ser Leu Thr Pro Pro Gln Leu Ala Thr Pro Asn Leu Gln Gln Phe
                140                 145                 150
Phe Pro Gln Ala Thr Arg Gln Ser Leu Leu Gly Pro Pro Pro Val
```

```
                155                 160                 165
Gly Val Pro Met Asn Pro Ser Gln Phe Asn Leu Ser Gly Arg Asn
                170                 175                 180
Pro Gln Lys Gln Ala Arg Thr Ser Ser Ser Thr Thr Pro Asn Arg
                185                 190                 195
Lys Asp Ser Ser Ser Gln Thr Met Pro Val Glu Asp Lys Ser Asp
                200                 205                 210
Pro Pro Glu Gly Ser Glu Glu Ala Ala Glu Pro Arg Met Asp Thr
                215                 220                 225
Pro Glu Asp Gln Asp Leu Pro Pro Cys Pro Glu Asp Ile Ala Lys
                230                 235                 240
Glu Lys Arg Thr Pro Ala Pro Glu Pro Glu Pro Cys Glu Ala Ser
                245                 250                 255
Glu Leu Pro Ala Lys Arg Leu Arg Ser Ser Glu Glu Pro Thr Glu
                260                 265                 270
Lys Glu Pro Pro Gly Gln Leu Gln Val Lys Ala Gln Pro Gln Ala
                275                 280                 285
Arg Met Thr Val Pro Lys Gln Thr Gln Thr Pro Asp Leu Leu Pro
                290                 295                 300
Glu Ala Leu Glu Ala Gln Val Leu Pro Arg Phe Gln Pro Arg Val
                305                 310                 315
Leu Gln Val Gln Ala Gln Val Gln Ser Gln Thr Gln Pro Arg Ile
                320                 325                 330
Pro Ser Thr Asp Thr Gln Val Gln Pro Lys Leu Gln Lys Gln Ala
                335                 340                 345
Gln Thr Gln Thr Ser Pro Glu His Leu Val Leu Gln Gln Lys Gln
                350                 355                 360
Val Gln Pro Gln Leu Gln Gln Glu Ala Glu Pro Gln Lys Gln Val
                365                 370                 375
Gln Pro Gln Val Gln Pro Gln Ala His Ser Gln Gly Pro Arg Gln
                380                 385                 390
Val Gln Leu Gln Gln Glu Ala Glu Pro Leu Lys Gln Val Gln Pro
                395                 400                 405
Gln Val Gln Pro Gln Ala His Ser Gln Pro Pro Arg Gln Val Gln
                410                 415                 420
Leu Gln Leu Gln Lys Gln Val Gln Thr Gln Thr Tyr Pro Gln Val
                425                 430                 435
His Thr Gln Ala Gln Pro Ser Val Gln Pro Gln Glu His Pro Pro
                440                 445                 450
Ala Gln Val Ser Val Gln Pro Pro Glu Gln Thr His Glu Gln Pro
                455                 460                 465
His Thr Gln Pro Gln Val Ser Leu Leu Ala Pro Glu Gln Thr Pro
                470                 475                 480
Val Val Val His Val Cys Gly Leu Glu Met Pro Pro Asp Ala Val
                485                 490                 495
Glu Ala Gly Gly Gly Met Glu Lys Thr Leu Pro Glu Pro Val Gly
                500                 505                 510
Thr Gln Val Ser Met Glu Glu Ile Gln Asn Glu Ser Ala Cys Gly
                515                 520                 525
Leu Asp Val Gly Glu Cys Glu Asn Arg Ala Arg Glu Met Pro Gly
                530                 535                 540
Val Trp Gly Ala Gly Gly Ser Leu Lys Val Thr Ile Leu Gln Ser
                545                 550                 555
Ser Asp Ser Arg Ala Phe Ser Thr Val Pro Leu Thr Pro Val Pro
                560                 565                 570
Arg Pro Ser Asp Ser Val Ser Ser Thr Pro Ala Ala Thr Ser Thr
                575                 580                 585
Pro Ser Lys Gln Ala Leu Gln Phe Phe Cys Tyr Ile Cys Lys Ala
                590                 595                 600
Ser Cys Ser Ser Gln Gln Glu Phe Gln Asp His Met Ser Glu Pro
                605                 610                 615
Gln His Gln Gln Arg Leu Gly Glu Ile Gln His Met Ser Gln Ala
                620                 625                 630
```

Cys Leu Leu Ser Leu Leu Pro Val Pro Arg Asp Val Leu Glu Thr
635 640 645
Glu Asp Glu Glu Pro Pro Pro Arg Arg Trp Cys Asn Thr Cys Gln
650 655 660
Leu Tyr Tyr Met Gly Asp Leu Ile Gln His Arg Arg Thr Gln Asp
665 670 675
His Lys Ile Ala Lys Gln Ser Leu Arg Pro Phe Cys Thr Val Cys
680 685 690
Asn Arg Tyr Phe Lys Thr Pro Arg Lys Phe Val Glu His Val Lys
695 700 705
Ser Gln Gly His Lys Asp Lys Ala Lys Glu Leu Lys Ser Leu Glu
710 715 720
Lys Glu Ile Ala Gly Gln Asp Glu Asp His Phe Ile Thr Val Asp
725 730 735
Ala Val Gly Cys Phe Glu Gly Asp Glu Glu Glu Glu Glu Asp Asp
740 745 750
Glu Asp Glu Glu Glu Ile Glu Val Glu Glu Glu Leu Cys Ser Arg
755 760 765

<210> 48
<211> 352
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1876258CD1

<400> 48
Met Pro Arg Ser Phe Leu Val Lys Ser Arg Lys Ala His Thr Tyr
1 5 10 15
His Gln Pro Arg Val Gln Glu Asp Glu Pro Leu Trp Pro Pro Ala
20 25 30
Leu Thr Pro Val Pro Arg Asp Gln Ala Pro Ser Asn Ser Pro Val
35 40 45
Leu Ser Thr Leu Phe Pro Asn Gln Cys Leu Asp Trp Thr Asn Leu
50 55 60
Lys Arg Glu Pro Glu Leu Glu Gln Asp Gln Asn Leu Ala Arg Met
65 70 75
Ala Pro Ala Pro Glu Gly Pro Ile Val Leu Ser Arg Pro Gln Asp
80 85 90
Gly Asp Ser Pro Leu Ser Asp Ser Pro Pro Phe Tyr Lys Pro Ser
95 100 105
Phe Ser Trp Asp Thr Leu Ala Thr Thr Tyr Gly His Ser Tyr Arg
110 115 120
Gln Ala Pro Ser Thr Met Gln Ser Ala Phe Leu Glu His Ser Val
125 130 135
Ser Leu Tyr Gly Ser Pro Leu Val Pro Ser Thr Glu Pro Ala Leu
140 145 150
Asp Phe Ser Leu Arg Tyr Ser Pro Gly Met Asp Ala Tyr His Cys
155 160 165
Val Lys Cys Asn Lys Val Phe Ser Thr Pro His Gly Leu Glu Val
170 175 180
His Val Arg Arg Ser His Ser Gly Thr Arg Pro Phe Ala Cys Asp
185 190 195
Ile Cys Gly Lys Thr Phe Gly His Ala Val Ser Leu Glu Gln His
200 205 210
Thr His Val His Ser Gln Gly Ile Pro Ala Gly Ser Ser Pro Glu
215 220 225
Pro Ala Pro Asp Pro Pro Gly Pro His Phe Leu Arg Gln Glu Arg
230 235 240
Ser Phe Glu Cys Arg Met Cys Gly Lys Thr Phe Lys Arg Ser Ser

```
                245                 250                 255
Thr Leu Ser Thr His Leu Leu Ile His Ser Asp Thr Arg Pro Tyr
                260                 265                 270
Pro Cys Gln Phe Cys Gly Lys Arg Phe His Gln Lys Ser Asp Met
                275                 280                 285
Lys Lys His Thr Tyr Ile His Thr Gly Glu Lys Pro His Lys Cys
                290                 295                 300
Gln Val Cys Gly Lys Ala Phe Ser Gln Ser Ser Asn Leu Ile Thr
                305                 310                 315
His Ser Arg Lys His Thr Gly Phe Lys Pro Phe Ser Cys Glu Leu
                320                 325                 330
Cys Thr Lys Gly Phe Gln Arg Lys Val Asp Leu Arg Arg His Arg
                335                 340                 345
Glu Ser Gln His Asn Leu Lys
                350

<210> 49
<211> 1102
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1929822CD1

<400> 49
Met Phe Gln Leu Pro Val Asn Asn Leu Gly Ser Leu Arg Lys Ala
  1               5                  10                  15
Arg Lys Thr Val Lys Lys Ile Leu Ser Asp Ile Gly Leu Glu Tyr
                 20                  25                  30
Cys Lys Glu His Ile Glu Asp Phe Lys Gln Phe Glu Pro Asn Asp
                 35                  40                  45
Phe Tyr Leu Lys Asn Thr Thr Trp Glu Asp Val Gly Leu Trp Asp
                 50                  55                  60
Pro Ser Leu Thr Lys Asn Gln Asp Tyr Arg Thr Lys Pro Phe Cys
                 65                  70                  75
Cys Ser Ala Cys Pro Phe Ser Ser Lys Phe Phe Ser Ala Tyr Lys
                 80                  85                  90
Ser His Phe Arg Asn Val His Ser Glu Asp Phe Glu Asn Arg Ile
                 95                 100                 105
Leu Leu Asn Cys Pro Tyr Cys Thr Phe Asn Ala Asp Lys Lys Thr
                110                 115                 120
Leu Glu Thr His Ile Lys Ile Phe His Ala Pro Asn Ala Ser Ala
                125                 130                 135
Pro Ser Ser Ser Leu Ser Thr Phe Lys Asp Lys Asn Lys Asn Asp
                140                 145                 150
Gly Leu Lys Pro Lys Gln Ala Asp Ser Val Glu Gln Ala Val Tyr
                155                 160                 165
Tyr Cys Lys Lys Cys Thr Tyr Arg Asp Pro Leu Tyr Glu Ile Val
                170                 175                 180
Arg Lys His Ile Tyr Arg Glu His Phe Gln His Val Ala Ala Pro
                185                 190                 195
Tyr Ile Ala Lys Ala Gly Glu Lys Ser Leu Asn Gly Ala Val Pro
                200                 205                 210
Leu Gly Ser Asn Ala Arg Glu Glu Ser Ser Ile His Cys Lys Arg
                215                 220                 225
Cys Leu Phe Met Pro Lys Ser Tyr Glu Ala Leu Val Gln His Val
                230                 235                 240
Ile Glu Asp His Glu Arg Ile Gly Tyr Gln Val Thr Ala Met Ile
                245                 250                 255
Gly His Thr Asn Val Val Val Pro Arg Ser Lys Pro Leu Met Leu
                260                 265                 270
Ile Ala Pro Lys Pro Gln Asp Lys Lys Ser Met Gly Leu Pro Pro
```

```
                275                 280                 285
Arg Ile Gly Ser Leu Ala Ser Gly Asn Val Arg Ser Leu Pro Ser
                290                 295                 300
Gln Gln Met Val Asn Arg Leu Ser Ile Pro Lys Pro Asn Leu Asn
                305                 310                 315
Ser Thr Gly Val Asn Met Met Ser Ser Val His Leu Gln Gln Asn
                320                 325                 330
Asn Tyr Gly Val Lys Ser Val Gly Gln Gly Tyr Ser Val Gly Gln
                335                 340                 345
Ser Met Arg Leu Gly Leu Gly Gly Asn Ala Pro Val Ser Ile Pro
                350                 355                 360
Gln Gln Ser Gln Ser Val Lys Gln Leu Leu Pro Ser Gly Asn Gly
                365                 370                 375
Arg Ser Tyr Gly Leu Gly Ser Glu Gln Arg Ser Gln Ala Pro Ala
                380                 385                 390
Arg Tyr Ser Leu Gln Ser Ala Asn Ala Ser Ser Leu Ser Ser Gly
                395                 400                 405
Gln Leu Lys Ser Pro Ser Leu Ser Gln Ser Gln Ala Ser Arg Val
                410                 415                 420
Leu Gly Gln Ser Ser Ser Lys Pro Ala Ala Ala Ala Thr Gly Pro
                425                 430                 435
Pro Pro Gly Asn Thr Ser Ser Thr Gln Lys Trp Lys Ile Cys Thr
                440                 445                 450
Ile Cys Asn Glu Leu Phe Pro Glu Asn Val Tyr Ser Val His Phe
                455                 460                 465
Glu Lys Glu His Lys Ala Glu Lys Val Pro Ala Val Ala Asn Tyr
                470                 475                 480
Ile Met Lys Ile His Asn Phe Thr Ser Lys Cys Leu Tyr Cys Asn
                485                 490                 495
Arg Tyr Leu Pro Thr Asp Thr Leu Leu Asn His Met Leu Ile His
                500                 505                 510
Gly Leu Ser Cys Pro Tyr Cys Arg Ser Thr Phe Asn Asp Val Glu
                515                 520                 525
Lys Met Ala Ala His Met Arg Met Val His Ile Asp Glu Glu Met
                530                 535                 540
Gly Pro Lys Thr Asp Ser Thr Leu Ser Phe Asp Leu Thr Leu Gln
                545                 550                 555
Gln Gly Ser His Thr Asn Ile His Leu Leu Val Thr Thr Tyr Asn
                560                 565                 570
Leu Arg Asp Ala Pro Ala Glu Ser Val Ala Tyr His Ala Gln Asn
                575                 580                 585
Asn Pro Pro Val Pro Pro Lys Pro Gln Pro Lys Val Gln Glu Lys
                590                 595                 600
Ala Asp Ile Pro Val Lys Ser Ser Pro Gln Ala Ala Val Pro Tyr
                605                 610                 615
Lys Lys Asp Val Gly Lys Thr Leu Cys Pro Leu Cys Phe Ser Ile
                620                 625                 630
Leu Lys Gly Pro Ile Ser Asp Ala Leu Ala His His Leu Arg Glu
                635                 640                 645
Arg His Gln Val Ile Gln Thr Val His Pro Val Glu Lys Lys Leu
                650                 655                 660
Thr Tyr Lys Cys Ile His Cys Leu Gly Val Tyr Thr Ser Asn Met
                665                 670                 675
Thr Ala Ser Thr Ile Thr Leu His Leu Val His Cys Arg Gly Val
                680                 685                 690
Gly Lys Thr Gln Asn Gly Gln Asp Lys Thr Asn Ala Pro Ser Arg
                695                 700                 705
Leu Asn Gln Ser Pro Ser Leu Ala Pro Val Lys Arg Thr Tyr Glu
                710                 715                 720
Gln Met Glu Phe Pro Leu Leu Lys Lys Arg Lys Leu Asp Asp Asp
                725                 730                 735
Ser Asp Ser Pro Ser Phe Phe Glu Glu Lys Pro Glu Glu Pro Val
                740                 745                 750
```

```
Val Leu Ala Leu Asp Pro Lys Gly His Glu Asp Asp Ser Tyr Glu
                755                 760                 765
Ala Arg Lys Ser Phe Leu Thr Lys Tyr Phe Asn Lys Gln Pro Tyr
                770                 775                 780
Pro Thr Arg Arg Glu Ile Glu Lys Leu Ala Ala Ser Leu Trp Leu
                785                 790                 795
Trp Lys Ser Asp Ile Ala Ser His Phe Ser Asn Lys Arg Lys Lys
                800                 805                 810
Cys Val Arg Asp Cys Glu Lys Tyr Lys Pro Gly Val Leu Leu Gly
                815                 820                 825
Phe Asn Met Lys Glu Leu Asn Lys Val Lys His Glu Met Asp Phe
                830                 835                 840
Asp Ala Glu Trp Leu Phe Glu Asn His Asp Glu Lys Asp Ser Arg
                845                 850                 855
Val Asn Ala Ser Lys Thr Ala Asp Lys Lys Leu Asn Leu Gly Lys
                860                 865                 870
Glu Asp Asp Ser Ser Ser Asp Ser Phe Glu Asn Leu Glu Glu Glu
                875                 880                 885
Ser Asn Glu Ser Gly Ser Pro Phe Asp Pro Val Phe Glu Val Glu
                890                 895                 900
Pro Lys Ile Ser Asn Asp Asn Pro Glu Glu His Val Leu Lys Val
                905                 910                 915
Ile Pro Glu Asp Ala Ser Glu Ser Glu Glu Lys Leu Asp Gln Lys
                920                 925                 930
Glu Asp Gly Ser Lys Tyr Glu Thr Ile His Leu Thr Glu Glu Pro
                935                 940                 945
Thr Lys Leu Met His Asn Ala Ser Asp Ser Glu Val Asp Gln Asp
                950                 955                 960
Asp Val Val Glu Trp Lys Asp Gly Ala Ser Pro Ser Glu Ser Gly
                965                 970                 975
Pro Gly Ser Gln Gln Val Ser Asp Phe Glu Asp Asn Thr Cys Glu
                980                 985                 990
Met Lys Pro Gly Thr Trp Ser Asp Glu Ser Ser Gln Ser Glu Asp
                995                1000                1005
Ala Arg Ser Ser Lys Pro Ala Ala Lys Lys Lys Ala Thr Met Gln
               1010                1015                1020
Gly Asp Arg Glu Gln Leu Lys Trp Lys Asn Ser Ser Tyr Gly Lys
               1025                1030                1035
Val Glu Gly Phe Trp Ser Lys Asp Gln Ser Gln Trp Lys Asn Ala
               1040                1045                1050
Ser Glu Asn Asp Glu Arg Leu Ser Asn Pro Gln Ile Glu Trp Gln
               1055                1060                1065
Asn Ser Thr Ile Asp Ser Glu Asp Gly Glu Gln Phe Asp Asn Met
               1070                1075                1080
Thr Asp Gly Val Ala Glu Pro Met His Gly Ser Leu Ala Gly Val
               1085                1090                1095
Lys Leu Ser Ser Gln Gln Ala
               1100

<210> 50
<211> 121
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1970095CD1

<400> 50
Met Gly Arg Ile Phe Leu Asp His Ile Gly Gly Thr Arg Leu Phe
  1               5                  10                  15
Ser Cys Ala Asn Cys Asp Thr Ile Leu Thr Asn Arg Ser Glu Leu
                 20                  25                  30
```

```
Ile Ser Thr Arg Phe Thr Gly Ala Thr Gly Arg Ala Phe Leu Phe
                35                  40                  45
Asn Lys Val Val Asn Leu Gln Tyr Ser Glu Val Gln Asp Arg Val
                50                  55                  60
Met Leu Thr Gly Arg His Met Val Arg Asp Val Ser Cys Lys Asn
                65                  70                  75
Cys Asn Ser Lys Leu Gly Trp Ile Tyr Glu Phe Ala Thr Glu Asp
                80                  85                  90
Ser Gln Arg Tyr Lys Glu Gly Arg Val Ile Leu Glu Arg Ala Leu
                95                  100                 105
Val Arg Glu Ser Glu Gly Phe Glu Glu His Val Pro Ser Asp Asn
                110                 115                 120
Ser
```

<210> 51
<211> 233
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1975473CD1

<400> 51

```
Met Pro Gly Pro Gly Thr Leu Ser Val Arg Val Ser Pro Pro Gln
 1               5                  10                  15
Pro Ile Leu Ser Arg Gly Arg Pro Asp Ser Asn Lys Thr Glu Asn
                20                  25                  30
Arg Arg Ile Thr His Ile Ser Ala Glu Gln Lys Arg Arg Phe Asn
                35                  40                  45
Ile Lys Leu Gly Phe Asp Thr Leu His Gly Leu Val Ser Thr Leu
                50                  55                  60
Ser Ala Gln Pro Ser Leu Lys Val Ser Lys Ala Thr Thr Leu Gln
                65                  70                  75
Lys Thr Ala Glu Tyr Ile Leu Met Leu Gln Gln Glu Arg Ala Gly
                80                  85                  90
Leu Gln Glu Glu Ala Gln Gln Leu Arg Asp Glu Ile Glu Glu Leu
                95                  100                 105
Asn Ala Ala Ile Asn Leu Cys Gln Gln Gln Leu Pro Ala Thr Gly
                110                 115                 120
Val Pro Ile Thr His Gln Arg Phe Asp Gln Met Arg Asp Met Phe
                125                 130                 135
Asp Asp Tyr Val Arg Thr Arg Thr Leu His Asn Trp Lys Phe Trp
                140                 145                 150
Val Phe Ser Ile Leu Ile Arg Pro Leu Phe Glu Ser Phe Asn Gly
                155                 160                 165
Met Val Ser Thr Ala Ser Val His Thr Leu Arg Gln Thr Ser Leu
                170                 175                 180
Ala Trp Leu Asp Gln Tyr Cys Ser Leu Pro Ala Leu Arg Pro Thr
                185                 190                 195
Val Leu Asn Ser Leu Arg Gln Leu Gly Thr Ser Thr Ser Ile Leu
                200                 205                 210
Thr Asp Pro Gly Arg Ile Pro Glu Gln Ala Thr Arg Ala Val Thr
                215                 220                 225
Glu Gly Thr Leu Gly Lys Pro Leu
                230
```

<210> 52
<211> 147
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1976527CD1

<400> 52
Met Ala Glu Arg Pro Glu Asp Leu Asn Leu Pro Asn Ala Val Ile
1 5 10 15
Thr Arg Ile Ile Lys Glu Ala Leu Pro Asp Gly Val Asn Ile Ser
20 25 30
Lys Glu Ala Arg Ser Ala Ile Ser Arg Ala Ala Ser Val Phe Val
35 40 45
Leu Tyr Ala Thr Ser Cys Ala Asn Asn Phe Ala Met Lys Gly Lys
50 55 60
Arg Lys Thr Leu Asn Ala Ser Asp Val Leu Ser Ala Met Glu Glu
65 70 75
Met Glu Phe Gln Arg Phe Val Thr Pro Leu Lys Glu Ala Leu Glu
80 85 90
Ala Tyr Arg Arg Glu Gln Lys Gly Lys Lys Glu Ala Ser Glu Gln
95 100 105
Lys Lys Lys Asp Lys Asp Lys Lys Thr Asp Ser Glu Glu Gln Asp
110 115 120
Lys Ser Arg Asp Glu Asp Asn Asp Glu Asp Glu Glu Arg Leu Glu
125 130 135
Glu Glu Glu Gln Asn Glu Glu Glu Glu Val Asp Asn
140 145

<210> 53
<211> 96
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2108023CD1

<400> 53
Met Ala Glu Val Glu Glu Thr Leu Lys Arg Ile Gln Ser His Lys
1 5 10 15
Gly Val Ile Gly Thr Met Val Val Asn Ala Glu Gly Ile Pro Ile
20 25 30
Arg Thr Thr Leu Asp Asn Ser Thr Thr Val Gln Tyr Ala Gly Leu
35 40 45
Leu His His Leu Thr Met Lys Ala Lys Ser Thr Val Arg Asp Ile
50 55 60
Asp Pro Gln Asn Asp Leu Thr Phe Leu Arg Ile Arg Ser Lys Lys
65 70 75
His Glu Ile Met Val Ala Pro Asp Lys Glu Tyr Leu Leu Ile Val
80 85 90
Ile Gln Asn Pro Cys Glu
95

<210> 54
<211> 259
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2135746CD1

<400> 54
Met Arg Asp Arg Arg Gly Pro Leu Gly Thr Cys Leu Ala Gln Val
1 5 10 15

```
Gln Gln Ala Gly Gly Gly Asp Ser Asp Lys Leu Ser Cys Ser Leu
                20                  25                  30
Lys Lys Arg Met Pro Glu Gly Pro Trp Pro Ala Asp Ala Pro Ser
                35                  40                  45
Trp Met Asn Lys Pro Val Val Asp Gly Asn Ser Gln Ser Glu Ala
                50                  55                  60
Leu Ser Leu Glu Met Arg Lys Asp Pro Ser Gly Ala Gly Leu Trp
                65                  70                  75
Leu His Ser Gly Gly Pro Val Leu Pro Tyr Val Arg Glu Ser Val
                80                  85                  90
Arg Arg Asn Pro Ala Ser Ala Ala Thr Pro Ser Thr Ala Val Gly
                95                  100                 105
Leu Phe Pro Ala Pro Thr Glu Cys Phe Ala Arg Val Ser Cys Ser
                110                 115                 120
Gly Val Glu Ala Leu Gly Arg Arg Asp Trp Leu Gly Gly Gly Pro
                125                 130                 135
Arg Ala Thr Asp Gly His Arg Gly Gln Cys Pro Lys Gly Glu Pro
                140                 145                 150
Arg Val Ser Arg Leu Pro Arg His Gln Lys Leu Pro Glu Met Gly
                155                 160                 165
Ser Phe Gln Asp Asp Pro Pro Ser Ala Phe Pro Lys Gly Leu Gly
                170                 175                 180
Ser Glu Leu Glu Pro Ala Cys Leu His Ser Ile Leu Ser Ala Thr
                185                 190                 195
Leu His Met Tyr Pro Glu Val Leu Leu Ser Glu Glu Thr Lys Arg
                200                 205                 210
Ile Phe Leu Asp Arg Leu Lys Pro Met Phe Ser Lys Gln Thr Ile
                215                 220                 225
Glu Phe Lys Lys Met Leu Lys Ser Thr Ser Asp Gly Leu Gln Ile
                230                 235                 240
Thr Leu Gly Leu Leu Ala Leu Gln Pro Phe Glu Leu Ala Asn Thr
                245                 250                 255
Leu Cys His Ser


<210> 55
<211> 474
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2154810CD1

<400> 55
Met Ala Leu Arg Ser Val Met Phe Ser Asp Val Ser Ile Asp Phe
  1               5                   10                  15
Ser Pro Glu Gly Trp Glu Tyr Leu Asp Leu Glu Gln Lys Asp Leu
                20                  25                  30
Tyr Arg Asp Val Met Leu Glu Asn Tyr Ser Asn Leu Val Ser Leu
                35                  40                  45
Gly Cys Phe Ile Ser Lys Pro Asp Val Ile Ser Ser Leu Glu Gln
                50                  55                  60
Gly Lys Glu Pro Trp Lys Val Val Arg Lys Gly Arg Arg Gln Tyr
                65                  70                  75
Pro Asp Leu Glu Thr Lys Tyr Glu Thr Lys Lys Leu Ser Leu Glu
                80                  85                  90
Asn Asp Ile Tyr Glu Ile Asn Leu Ser Gln Trp Lys Ile Met Glu
                95                  100                 105
Arg Ile Glu Asn His Gly Leu Lys Gly Leu Ile Leu Lys Asn Asp
                110                 115                 120
Trp Glu Ser Thr Gly Lys Ile Glu Gly Gln Glu Arg Pro Gln Glu
                125                 130                 135
```

```
Gly Tyr Phe Ser Ser Val Lys Met Pro Ser Glu Lys Val Ser Ser
                140                 145                 150
Tyr Gln Lys Arg Thr Ser Val Thr Pro His Gln Arg Leu His Phe
                155                 160                 165
Val Asp Lys Pro Tyr Glu Cys Lys Glu Cys Gly Lys Ala Phe Arg
                170                 175                 180
Val Arg Gln Gln Leu Thr Phe His His Arg Ile His Thr Gly Glu
                185                 190                 195
Lys Pro Tyr Glu Cys Lys Glu Cys Gly Met Ala Phe Arg Gln Thr
                200                 205                 210
Ala His Leu Thr Arg His Gln Arg Ile His Thr Gly Glu Lys Pro
                215                 220                 225
Tyr Glu Cys Lys Glu Cys Gly Lys Ala Phe Ser Arg Gly Tyr His
                230                 235                 240
Leu Ser Gln His Gln Lys Ile His Thr Gly Glu Lys Pro Phe Glu
                245                 250                 255
Cys Lys Glu Cys Gly Lys Ala Phe Ser Trp Gly Ser Ser Leu Val
                260                 265                 270
Lys His Glu Arg Val His Thr Gly Glu Lys Ser His Glu Cys Lys
                275                 280                 285
Glu Cys Gly Lys Thr Phe Cys Ser Gly Tyr Gln Leu Thr Arg His
                290                 295                 300
Gln Val Phe His Thr Gly Glu Lys Pro Tyr Glu Cys Lys Glu Cys
                305                 310                 315
Gly Lys Ala Phe Asn Cys Gly Ser Ser Leu Val Gln His Glu Arg
                320                 325                 330
Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Lys Glu Cys Gly Lys
                335                 340                 345
Ala Phe Ser Arg Gly Tyr His Leu Thr Gln His Gln Lys Ile His
                350                 355                 360
Thr Gly Glu Lys Pro Phe Lys Cys Lys Glu Cys Gly Lys Ala Phe
                365                 370                 375
Ser Trp Gly Ser Ser Leu Val Lys His Glu Arg Val His Thr Asn
                380                 385                 390
Glu Lys Ser Tyr Glu Cys Lys Asp Cys Gly Lys Ala Phe Gly Ser
                395                 400                 405
Gly Tyr Gln Leu Ser Val His Gln Arg Phe His Thr Gly Glu Lys
                410                 415                 420
Leu Tyr Gln His Lys Glu Phe Gly Lys Thr Phe Thr Arg Gly Ser
                425                 430                 435
Lys Leu Val His Glu Arg Thr His Ser Asn Asp Lys Pro Tyr Glu
                440                 445                 450
Cys Asn Glu Cys Gly Glu Ala Phe Leu Trp Thr Thr Tyr Ser Asn
                455                 460                 465
Glu Lys Ile Asp Thr Asp Glu Thr Leu
                470
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<210> 56
<211> 231
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2228991CD1

<400> 56

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Met Ser His Gly Asn Lys Glu Val Phe Ser Cys Arg Gly Ile Leu
  1               5                  10                  15
Leu Ala Val Asn Trp Phe Leu Glu Arg Gly His Thr Asp Ile Thr
                 20                  25                  30
Val Phe Val Pro Ser Trp Arg Lys Glu Gln Pro Arg Pro Asp Val
                 35                  40                  45
```

Pro Ile Thr Asp Gln His Ile Leu Arg Glu Leu Glu Lys Lys Lys
50 55 60
Ile Leu Val Phe Thr Pro Ser Arg Arg Val Gly Gly Lys Arg Val
65 70 75
Val Cys Tyr Asp Asp Arg Phe Ile Val Lys Leu Ala Tyr Glu Ser
80 85 90
Asp Gly Ile Val Val Ser Asn Asp Thr Tyr Arg Asp Leu Gln Gly
95 100 105
Glu Arg Gln Glu Trp Lys Arg Phe Ile Glu Glu Arg Leu Leu Met
110 115 120
Tyr Ser Phe Val Asn Asp Lys Phe Met Pro Pro Asp Asp Pro Leu
125 130 135
Gly Arg His Gly Pro Ser Leu Asp Asn Phe Leu Arg Lys Lys Pro
140 145 150
Leu Thr Leu Glu His Arg Lys Gln Pro Cys Pro Tyr Gly Arg Lys
155 160 165
Cys Thr Tyr Gly Ile Lys Cys Arg Phe Phe His Pro Glu Arg Pro
170 175 180
Ser Cys Pro Gln Arg Ser Val Ala Asp Glu Leu Arg Ala Asn Ala
185 190 195
Leu Leu Ser Pro Pro Arg Ala Pro Ser Lys Asp Lys Asn Gly Arg
200 205 210
Arg Pro Ser Pro Ser Ser Gln Ser Ser Ser Leu Leu Thr Glu Ser
215 220 225
Glu Gln Cys Ser Leu Asp
230

<210> 57
<211> 456
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2241206CD1

<400> 57
Met Asp Ser Arg Leu Gln Glu Ile Arg Glu Arg Gln Lys Leu Arg
1 5 10 15
Arg Gln Leu Leu Ala Gln Gln Leu Gly Ala Glu Ser Ala Asp Ser
20 25 30
Ile Gly Ala Val Leu Asn Ser Lys Asp Glu Gln Arg Glu Ile Ala
35 40 45
Glu Thr Arg Glu Thr Cys Arg Ala Ser Tyr Asp Thr Ser Ala Pro
50 55 60
Asn Ala Lys Arg Lys Tyr Leu Asp Glu Gly Glu Thr Asp Glu Asp
65 70 75
Lys Met Glu Glu Tyr Lys Asp Glu Leu Glu Met Gln Gln Asp Glu
80 85 90
Glu Asn Leu Pro Tyr Glu Glu Glu Ile Tyr Lys Asp Ser Ser Thr
95 100 105
Phe Leu Lys Gly Thr Gln Ser Leu Asn Pro His Asn Asp Tyr Cys
110 115 120
Gln His Phe Val Asp Thr Gly His Arg Pro Gln Asn Phe Ile Arg
125 130 135
Asp Val Gly Leu Ala Asp Arg Phe Glu Glu Tyr Pro Lys Leu Arg
140 145 150
Glu Leu Ile Arg Leu Lys Asp Glu Leu Ile Ala Lys Ser Asn Thr
155 160 165
Pro Pro Met Tyr Leu Gln Ala Asp Ile Glu Ala Phe Asp Ile Arg
170 175 180
Glu Leu Thr Pro Lys Phe Asp Val Ile Leu Leu Glu Pro Pro Leu
185 190 195

```
Glu Glu Tyr Tyr Arg Glu Thr Gly Ile Thr Ala Asn Glu Lys Cys
                200                 205                 210
Trp Thr Trp Asp Asp Ile Met Lys Leu Glu Ile Asp Glu Ile Ala
                215                 220                 225
Ala Pro Arg Ser Phe Ile Phe Leu Trp Cys Gly Ser Gly Glu Gly
                230                 235                 240
Leu Asp Leu Gly Arg Val Cys Leu Arg Lys Trp Gly Tyr Arg Arg
                245                 250                 255
Cys Glu Asp Ile Cys Trp Ile Lys Thr Asn Lys Asn Asn Pro Gly
                260                 265                 270
Lys Thr Lys Thr Leu Asp Pro Lys Ala Val Phe Gln Arg Thr Lys
                275                 280                 285
Glu His Cys Leu Met Gly Ile Lys Gly Thr Val Lys Arg Ser Thr
                290                 295                 300
Asp Gly Asp Phe Ile His Ala Asn Val Asp Ile Asp Leu Ile Ile
                305                 310                 315
Thr Glu Glu Pro Glu Ile Gly Asn Ile Glu Lys Pro Val Glu Ile
                320                 325                 330
Phe His Ile Ile Glu His Phe Cys Leu Gly Arg Arg Arg Leu His
                335                 340                 345
Leu Phe Gly Arg Asp Ser Thr Ile Arg Pro Gly Trp Leu Thr Val
                350                 355                 360
Gly Pro Thr Leu Thr Asn Ser Asn Tyr Asn Ala Glu Thr Tyr Ala
                365                 370                 375
Ser Tyr Phe Ser Ala Pro Asn Ser Tyr Leu Thr Gly Cys Thr Glu
                380                 385                 390
Glu Ile Glu Arg Leu Arg Pro Lys Ser Pro Pro Pro Lys Ser Lys
                395                 400                 405
Ser Asp Arg Gly Gly Gly Ala Pro Arg Gly Gly Gly Arg Gly Gly
                410                 415                 420
Thr Ser Ala Gly Arg Gly Arg Glu Arg Asn Arg Ser Asn Phe Arg
                425                 430                 435
Gly Glu Arg Gly Gly Phe Arg Gly Gly Arg Gly Gly Ala His Arg
                440                 445                 450
Gly Gly Phe Pro Pro Arg
                455

&lt;210&gt; 58
&lt;211&gt; 159
&lt;212&gt; PRT
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; misc_feature
&lt;223&gt; Incyte ID No: 2259590CD1

&lt;400&gt; 58
Met Ser Ala Ala Ile Pro Pro Pro Gln Ala Ser Ala Lys Pro Phe
 1               5                  10                  15
Leu Gly Pro Trp Arg Gln Pro Val Ser Ser Arg Arg Ala Glu Ala
                20                  25                  30
Ala Pro Arg Thr Leu Cys Ala Phe Tyr Thr Thr Ala Gly Thr Glu
                35                  40                  45
Val Pro Arg Ser Pro Glu Pro Glu Pro Gly Val Gly Arg Ala Arg
                50                  55                  60
Arg Thr Gly Phe Leu Ala Asp Ser His Gly Leu Thr Gln Pro Pro
                65                  70                  75
Gly Pro Met Ala Ala Pro Ala Leu Ala Leu Val Ser Phe Glu Asp
                80                  85                  90
Val Val Val Thr Phe Thr Gly Glu Glu Trp Gly His Leu Asp Leu
                95                  100                 105
Ala Gln Arg Thr Leu Tyr Gln Glu Val Met Leu Glu Thr Cys Arg
                110                 115                 120
```

Leu Leu Val Ser Leu Gly His Pro Val Pro Lys Pro Glu Leu Ile
125 130 135
Tyr Leu Leu Glu His Gly Gln Glu Leu Trp Thr Val Lys Arg Gly
140 145 150
Leu Ser Gln Ser Thr Cys Ala Gly Trp
155

<210> 59
<211> 260
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2307537CD1

<400> 59
Met Pro Val Asp Phe Cys Thr Thr Arg Val Ser Pro Ala His Arg
1 5 10 15
Ser Pro Thr Val Leu Cys Gln Lys Val Cys Glu Glu Asn Ser Val
20 25 30
Ser Pro Ile Gly Cys Asn Ser Ser Asp Pro Ala Asp Phe Glu Pro
35 40 45
Ile Pro Ser Phe Ser Gly Phe Pro Leu Asp Ser Pro Lys Thr Leu
50 55 60
Val Leu Asp Phe Glu Thr Glu Gly Glu Arg Asn Ser Pro Asn Pro
65 70 75
Arg Ser Val Arg Ile Pro Ser Pro Asn Ile Leu Lys Thr Gly Leu
80 85 90
Thr Glu Asn Val Asp Arg Gly Leu Gly Gly Leu Glu Gly Thr His
95 100 105
Gln Ala Leu Asp Leu Leu Ala Gly Gly Met Met Pro Glu Glu Val
110 115 120
Lys Glu Ser Ser Gln Leu Asp Lys Gln Glu Ser Leu Gly Leu Glu
125 130 135
Leu Lys Thr Ile Asn Ser Ala Gly Leu Gly Pro Ser Pro Cys Leu
140 145 150
Pro Asp Leu Val Asp Phe Val Thr Arg Thr Ser Gly Val Gln Lys
155 160 165
Asp Lys Leu Cys Ser Pro Leu Ser Glu Pro Gly Asp Pro Ser Lys
170 175 180
Cys Ser Ser Leu Glu Leu Gly Pro Leu Gln Leu Glu Ile Ser Asn
185 190 195
Ala Ser Thr Thr Glu Val Ala Ile Leu Gln Val Asp Asp Asp Ser
200 205 210
Gly Asp Pro Leu Asn Leu Val Lys Ala Pro Val Ser Arg Ser Pro
215 220 225
Pro Arg Glu Gln Val Ile Glu Asp Asn Met Val Pro Gln Gly Met
230 235 240
Pro Glu Gln Glu Thr Thr Val Gly Ala Ile Gln Asp His Thr Glu
245 250 255
Ser Ser Val His Asn
260

<210> 60
<211> 352
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2440675CD1

<400> 60
Met Pro Arg Ser Phe Leu Val Lys Ser Arg Lys Ala His Thr Tyr
1 5 10 15
His Gln Pro Arg Val Gln Glu Asp Glu Pro Leu Trp Pro Pro Ala
20 25 30
Leu Thr Pro Val Pro Arg Asp Gln Ala Pro Ser Asn Ser Pro Val
35 40 45
Leu Ser Thr Leu Phe Pro Asn Gln Cys Leu Asp Trp Thr Asn Leu
50 55 60
Lys Arg Glu Pro Glu Leu Glu Gln Asp Gln Asn Leu Ala Arg Met
65 70 75
Ala Pro Ala Pro Glu Gly Pro Ile Val Leu Ser Arg Pro Gln Asp
80 85 90
Gly Asp Ser Pro Leu Ser Asp Ser Pro Pro Phe Tyr Lys Pro Ser
95 100 105
Phe Ser Trp Asp Thr Leu Ala Thr Thr Tyr Gly His Ser Tyr Arg
110 115 120
Gln Ala Pro Ser Thr Met Gln Ser Ala Phe Leu Glu His Ser Val
125 130 135
Ser Leu Tyr Gly Ser Pro Leu Val Pro Ser Thr Glu Pro Ala Leu
140 145 150
Asp Phe Ser Leu Arg Tyr Ser Pro Gly Met Asp Ala Tyr His Cys
155 160 165
Val Lys Cys Asn Lys Val Phe Ser Thr Pro His Gly Leu Glu Val
170 175 180
His Val Arg Arg Ser His Ser Gly Thr Arg Pro Phe Ala Cys Asp
185 190 195
Ile Cys Gly Lys Thr Phe Gly His Ala Val Ser Leu Glu Gln His
200 205 210
Thr His Val His Ser Gln Gly Ile Pro Ala Gly Ser Ser Pro Glu
215 220 225
Pro Ala Pro Asp Pro Pro Gly Pro His Phe Leu Arg Gln Glu Arg
230 235 240
Ser Phe Glu Cys Arg Met Cys Gly Lys Thr Phe Lys Arg Ser Ser
245 250 255
Thr Leu Ser Thr His Leu Leu Ile His Ser Asp Thr Arg Pro Tyr
260 265 270
Pro Cys Gln Phe Cys Gly Lys Arg Phe His Gln Lys Ser Asp Met
275 280 285
Lys Lys His Thr Tyr Ile His Thr Gly Glu Lys Pro His Lys Cys
290 295 300
Gln Val Cys Gly Lys Ala Phe Ser Gln Ser Ser Asn Leu Ile Thr
305 310 315
His Ser Arg Lys His Thr Gly Phe Lys Pro Phe Ser Cys Glu Leu
320 325 330
Cys Thr Lys Gly Phe Gln Arg Lys Val Asp Leu Arg Arg His Arg
335 340 345
Glu Ser Gln His Asn Leu Lys
350

<210> 61
<211> 467
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2463542CD1

<400> 61
Met Arg Thr Tyr Val Cys His Ile Cys Ser Ile Ala Phe Thr Ser
1 5 10 15
Leu Asp Met Phe Arg Ser His Met Gln Gly Gly Glu His Gln Ile

20 25 30
Lys Glu Ser Ile Val Ile Asn Leu Val Lys Asn Ser Arg Lys Thr
35 40 45
Gln Asp Ser Tyr Gln Asn Glu Cys Ala Asp Tyr Ile Asn Val Gln
50 55 60
Lys Ala Arg Gly Leu Glu Ala Lys Thr Cys Phe Arg Lys Met Glu
65 70 75
Glu Ser Ser Leu Glu Thr Cys Arg Tyr Arg Glu Val Val Asp Ser
80 85 90
Arg Pro Arg His Arg Met Phe Glu Gln Arg Leu Pro Phe Glu Thr
95 100 105
Phe Arg Thr Tyr Ala Ala Pro Tyr Asn Ile Ser Gln Ala Met Glu
110 115 120
Lys Gln Leu Pro His Ser Lys Lys Thr Tyr Asp Ser Phe Gln Asp
125 130 135
Glu Leu Glu Asp Tyr Ile Lys Val Gln Lys Ala Arg Gly Leu Asp
140 145 150
Pro Lys Thr Cys Phe Arg Lys Met Arg Glu Asn Ser Val Asp Thr
155 160 165
His Gly Tyr Arg Glu Met Val Asp Ser Gly Pro Arg Ser Arg Met
170 175 180
Cys Glu Gln Arg Phe Ser His Glu Ala Ser Gln Thr Tyr Gln Arg
185 190 195
Pro Tyr His Ile Ser Pro Val Glu Ser Gln Leu Pro Gln Trp Leu
200 205 210
Pro Thr His Ser Lys Arg Thr Tyr Asp Ser Phe Gln Asp Glu Leu
215 220 225
Glu Asp Tyr Ile Lys Val Gln Lys Ala Arg Gly Leu Glu Pro Lys
230 235 240
Thr Cys Phe Arg Lys Ile Gly Asp Ser Ser Val Glu Thr His Arg
245 250 255
Asn Arg Glu Met Val Asp Val Arg Pro Arg His Arg Met Leu Glu
260 265 270
Gln Lys Leu Pro Cys Glu Thr Phe Gln Thr Tyr Ser Gly Pro Tyr
275 280 285
Ser Ile Ser Gln Val Val Glu Asn Gln Leu Pro His Cys Leu Pro
290 295 300
Ala His Asp Ser Lys Gln Arg Leu Asp Ser Ile Ser Tyr Cys Gln
305 310 315
Leu Thr Arg Asp Cys Phe Pro Glu Lys Pro Val Pro Leu Ser Leu
320 325 330
Asn Gln Gln Glu Asn Asn Ser Gly Ser Tyr Ser Val Glu Ser Glu
335 340 345
Val Tyr Lys His Leu Ser Ser Glu Asn Asn Thr Ala Asp His Gln
350 355 360
Ala Gly His Lys Arg Lys His Gln Lys Arg Lys Arg His Leu Glu
365 370 375
Glu Gly Lys Glu Arg Pro Glu Lys Glu Gln Ser Lys His Lys Arg
380 385 390
Lys Lys Ser Tyr Glu Asp Thr Asp Leu Asp Lys Asp Lys Ser Ile
395 400 405
Arg Gln Arg Lys Arg Glu Glu Asp Arg Val Lys Val Ser Ser Gly
410 415 420
Lys Leu Lys His Arg Lys Lys Lys Lys Ser His Asp Val Pro Ser
425 430 435
Glu Lys Glu Glu Arg Lys His Arg Lys Glu Lys Lys Lys Ser Val
440 445 450
Glu Glu Arg Thr Glu Glu Glu Met Leu Trp Asp Glu Ser Ile Leu
455 460 465
Gly Phe

<210> 62

<211> 550
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2486031CD1

<400> 62
Met Val Arg Gly Trp Glu Pro Pro Pro Gly Leu Asp Cys Ala Ile
1 5 10 15
Ser Glu Gly His Lys Ser Glu Gly Thr Met Pro Pro Asn Lys Glu
20 25 30
Ala Ser Gly Leu Ser Ser Ser Pro Ala Gly Leu Ile Cys Leu Pro
35 40 45
Pro Ile Ser Glu Glu Leu Gln Leu Val Trp Thr Gln Ala Ala Gln
50 55 60
Thr Ser Glu Leu Asp Ser Asn Glu His Leu Leu Lys Thr Phe Ser
65 70 75
Tyr Phe Pro Tyr Pro Ser Leu Ala Asp Ile Ala Leu Leu Cys Leu
80 85 90
Arg Tyr Gly Leu Gln Met Glu Lys Val Lys Thr Trp Phe Met Ala
95 100 105
Gln Arg Leu Arg Cys Gly Ile Ser Trp Ser Ser Glu Glu Ile Glu
110 115 120
Glu Thr Arg Ala Arg Val Val Tyr Arg Arg Asp Gln Leu His Phe
125 130 135
Lys Ser Leu Leu Ser Phe Thr His His Ala Gly Arg Pro Pro Glu
140 145 150
Glu Val Pro Pro Pro Pro Val Pro Ala Pro Glu Gln Val Gly Ile
155 160 165
Gly Ile Gly Pro Pro Thr Leu Ser Lys Pro Thr Gln Thr Lys Gly
170 175 180
Leu Lys Val Glu Pro Glu Glu Pro Ser Gln Met Pro Pro Leu Pro
185 190 195
Gln Ser His Gln Lys Leu Lys Glu Ser Leu Met Thr Pro Gly Ser
200 205 210
Gly Ala Phe Pro Tyr Gln Ser Asp Phe Trp Gln His Leu Gln Ser
215 220 225
Ser Gly Leu Ser Lys Glu Gln Ala Gly Arg Gly Pro Asn Gln Ser
230 235 240
His Gly Ile Gly Thr Ala Ser Trp Asn His Ser Thr Thr Val Pro
245 250 255
Gln Pro Gln Ala Arg Asp Lys Pro Pro Pro Ile Ala Leu Ile Ala
260 265 270
Ser Ser Cys Lys Glu Glu Ser Ala Ser Ser Val Thr Pro Ser Ser
275 280 285
Ser Ser Thr Ser Ser Ser Phe Gln Val Leu Ala Asn Gly Ala Thr
290 295 300
Ala Thr Ser Lys Pro Leu Gln Pro Leu Gly Cys Val Pro Gln Ser
305 310 315
Val Ser Pro Ser Glu Gln Ala Leu Pro Pro His Leu Glu Pro Ala
320 325 330
Trp Pro Gln Gly Leu Arg His Asn Ser Val Pro Gly Arg Val Gly
335 340 345
Pro Thr Glu Tyr Leu Ser Pro Asp Met Gln Arg Gln Arg Lys Thr
350 355 360
Lys Arg Lys Thr Lys Glu Gln Leu Ala Ile Leu Lys Ser Phe Phe
365 370 375
Leu Gln Cys Gln Trp Ala Arg Arg Glu Asp Tyr Gln Lys Leu Glu
380 385 390
Gln Ile Thr Gly Leu Pro Arg Pro Glu Ile Ile Gln Trp Phe Gly
395 400 405

Asp Thr Arg Tyr Ala Leu Lys His Gly Gln Leu Lys Trp Phe Arg
410 415 420
Asp Asn Ala Val Pro Gly Ala Pro Ser Phe Gln Asp Pro Ala Ile
425 430 435
Pro Thr Pro Pro Pro Ser Thr Arg Ser Leu Asn Glu Arg Ala Glu
440 445 450
Thr Pro Pro Leu Pro Ile Pro Pro Pro Pro Pro Asp Ile Gln Pro
455 460 465
Leu Glu Arg Tyr Trp Ala Ala His Gln Gln Leu Arg Glu Thr Asp
470 475 480
Ile Pro Gln Leu Ser Gln Ala Ser Arg Leu Ser Thr Gln Gln Val
485 490 495
Leu Asp Trp Phe Asp Ser Arg Leu Pro Gln Pro Ala Glu Val Val
500 505 510
Val Cys Leu Asp Glu Glu Glu Glu Glu Glu Glu Glu Glu Leu Pro
515 520 525
Glu Asp Asp Glu Glu Glu Glu Glu Glu Glu Glu Glu Asp Asp Asp
530 535 540
Asp Asp Asp Asp Asp Val Ile Ile Gln Asp
545 550

<210> 63
<211> 450
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2493052CD1

<400> 63
Met Ala Ala Ser Lys Thr Gln Gly Ala Val Ala Arg Met Gln Glu
1 5 10 15
Asp Arg Asp Gly Ser Cys Ser Thr Val Gly Gly Val Gly Tyr Gly
20 25 30
Asp Ser Lys Asp Cys Ile Leu Glu Pro Leu Ser Leu Pro Glu Ser
35 40 45
Pro Gly Gly Thr Thr Thr Leu Glu Gly Ser Pro Ser Val Pro Cys
50 55 60
Ile Phe Cys Glu Glu His Phe Pro Val Ala Glu Gln Asp Lys Leu
65 70 75
Leu Lys His Met Ile Ile Glu His Lys Ile Val Ile Ala Asp Val
80 85 90
Lys Leu Val Ala Asp Phe Gln Arg Tyr Ile Leu Tyr Trp Arg Lys
95 100 105
Arg Phe Thr Glu Gln Pro Ile Thr Asp Phe Cys Ser Val Ile Arg
110 115 120
Ile Asn Ser Thr Ala Pro Phe Glu Glu Gln Glu Asn Tyr Phe Leu
125 130 135
Leu Cys Asp Val Leu Pro Glu Asp Arg Ile Leu Arg Glu Glu Leu
140 145 150
Gln Lys Gln Arg Leu Arg Glu Ile Leu Glu Gln Gln Gln Gln Glu
155 160 165
Arg Asn Asp Thr Asn Phe His Gly Val Cys Met Phe Cys Asn Glu
170 175 180
Glu Phe Leu Gly Asn Arg Ser Val Ile Leu Asn His Met Ala Arg
185 190 195
Glu His Ala Phe Asn Ile Gly Leu Pro Asp Asn Ile Val Asn Cys
200 205 210
Asn Glu Phe Leu Cys Thr Leu Gln Lys Lys Leu Asp Asn Leu Gln
215 220 225
Cys Leu Tyr Cys Glu Lys Thr Phe Arg Asp Lys Asn Thr Leu Lys
230 235 240

```
Asp His Met Arg Lys Lys Gln His Arg Lys Ile Asn Pro Lys Asn
                245                 250                 255
Arg Glu Tyr Asp Arg Phe Tyr Val Ile Asn Tyr Leu Glu Leu Gly
                260                 265                 270
Lys Ser Trp Glu Glu Val Gln Leu Glu Asp Asp Arg Glu Leu Leu
                275                 280                 285
Asp His Gln Glu Asp Asp Trp Ser Asp Trp Glu Glu His Pro Ala
                290                 295                 300
Ser Ala Val Cys Leu Phe Cys Glu Lys Gln Ala Glu Thr Ile Glu
                305                 310                 315
Lys Leu Tyr Val His Met Glu Asp Ala His Glu Phe Asp Leu Leu
                320                 325                 330
Lys Ile Lys Ser Glu Leu Gly Leu Asn Phe Tyr Gln Gln Val Lys
                335                 340                 345
Leu Val Asn Phe Ile Arg Arg Gln Val His Gln Cys Arg Cys Tyr
                350                 355                 360
Gly Cys His Val Lys Phe Lys Ser Lys Ala Asp Leu Arg Thr His
                365                 370                 375
Met Glu Glu Thr Lys His Thr Ser Leu Leu Pro Asp Arg Lys Thr
                380                 385                 390
Trp Asp Gln Leu Glu Tyr Tyr Phe Pro Thr Tyr Glu Asn Asp Thr
                395                 400                 405
Leu Leu Cys Thr Leu Ser Asp Ser Glu Ser Asp Leu Thr Ala Gln
                410                 415                 420
Glu Gln Asn Glu Asn Val Pro Ile Ile Ser Glu Asp Thr Ser Lys
                425                 430                 435
Leu Tyr Ala Leu Lys Gln Ser Ser Ile Leu Asn Gln Leu Leu Leu
                440                 445                 450


<210> 64
<211> 378
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2512074CD1

<400> 64
Met Ile Ser Phe Gln Glu Ser Val Thr Phe Gln Asp Val Ala Val
  1               5                  10                  15
Asp Phe Thr Ala Glu Glu Trp Gln Leu Leu Asp Cys Ala Glu Arg
                 20                  25                  30
Thr Leu Tyr Trp Asp Val Met Leu Glu Asn Tyr Arg Asn Leu Ile
                 35                  40                  45
Ser Val Gly Cys Pro Ile Thr Lys Thr Lys Val Ile Leu Lys Val
                 50                  55                  60
Glu Gln Gly Gln Glu Pro Trp Met Val Glu Gly Ala Asn Pro His
                 65                  70                  75
Glu Ser Ser Pro Glu Ser Asp Tyr Pro Leu Val Asp Glu Pro Gly
                 80                  85                  90
Lys His Arg Glu Ser Lys Asp Asn Phe Leu Lys Ser Val Leu Leu
                 95                 100                 105
Thr Phe Asn Lys Ile Leu Thr Met Glu Arg Ile His His Tyr Asn
                110                 115                 120
Met Ser Thr Ser Leu Asn Pro Met Arg Lys Lys Ser Tyr Lys Ser
                125                 130                 135
Phe Glu Lys Cys Leu Pro Pro Asn Leu Asp Leu Leu Lys Tyr Asn
                140                 145                 150
Arg Ser Tyr Thr Val Glu Asn Ala Tyr Glu Cys Ser Glu Cys Gly
                155                 160                 165
Lys Ala Phe Lys Lys Lys Phe His Phe Ile Arg His Glu Lys Asn
```

```
                170                 175                 180
His Thr Arg Lys Lys Pro Phe Glu Cys Asn Asp Cys Gly Lys Ala
                185                 190                 195
Tyr Ser Arg Lys Ala His Leu Ala Thr His Gln Lys Ile His Asn
                200                 205                 210
Gly Glu Arg Pro Phe Val Cys Asn Asp Cys Gly Lys Ala Phe Met
                215                 220                 225
His Lys Ala Gln Leu Val Val His Gln Arg Leu His Thr Gly Glu
                230                 235                 240
Lys Pro Tyr Glu Cys Ser Gln Cys Gly Lys Thr Phe Thr Trp Asn
                245                 250                 255
Ser Ser Phe Asn Gln His Val Lys Ser His Thr Leu Glu Lys Ser
                260                 265                 270
Phe Glu Cys Lys Glu Cys Gly Lys Thr Phe Arg Tyr Ser Ser Ser
                275                 280                 285
Leu Tyr Lys His Ser Arg Phe His Thr Gly Glu Lys Pro Tyr Gln
                290                 295                 300
Cys Ile Ile Cys Gly Lys Ala Phe Gly Asn Thr Ser Val Leu Val
                305                 310                 315
Thr His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Ser Cys Ile
                320                 325                 330
Glu Cys Gly Lys Ala Phe Ile Lys Lys Ser His Leu Leu Arg His
                335                 340                 345
Gln Ile Thr His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Arg Cys
                350                 355                 360
Gly Lys Ala Phe Ser Gln Lys Ser Asn Leu Ile Val His Gln Lys
                365                 370                 375
Ile His Thr


<210> 65
<211> 233
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2646274CD1

<400> 65
Met Pro Ile Leu Val Glu Lys Phe Pro Phe Val Arg Lys Ser Glu
  1               5                  10                  15
Arg Thr Leu Glu Cys Tyr Val His Asn Leu Leu Arg Ile Ser Val
                 20                  25                  30
Tyr Phe Pro Thr Leu Arg His Glu Ile Leu Glu Leu Ile Ile Glu
                 35                  40                  45
Lys Leu Leu Lys Leu Asp Val Asn Ala Ser Arg Gln Gly Ile Glu
                 50                  55                  60
Asp Ala Glu Glu Thr Ala Asn Gln Thr Cys Gly Gly Thr Asp Ser
                 65                  70                  75
Thr Glu Gly Leu Phe Asn Met Gly Phe Ala Glu Ala Phe Leu Glu
                 80                  85                  90
His Leu Trp Lys Asn Leu Gln Asp Pro Ser Asn Pro Ala Ile Ile
                 95                 100                 105
Arg Gln Ala Ala Gly Asn Tyr Ile Gly Ser Phe Leu Ala Arg Ala
                110                 115                 120
Lys Phe Ile Ser Leu Ile Thr Val Lys Pro Cys Leu Asp Leu Leu
                125                 130                 135
Val Asn Trp Leu His Ile Tyr Leu Asn Asn Gln Asp Ser Gly Thr
                140                 145                 150
Lys Ala Phe Cys Asp Val Ala Leu His Gly Pro Phe Tyr Ser Ala
                155                 160                 165
Cys Gln Ala Val Phe Tyr Thr Phe Val Phe Arg His Lys Gln Leu
```

```
                170                 175                 180
Leu Ser Gly Asn Leu Lys Glu Gly Leu Gln Tyr Pro Gln Ser Leu
                185                 190                 195
Asn Phe Glu Arg Ile Val Met Ser Gln Leu Asn Pro Leu Lys Ile
                200                 205                 210
Cys Leu Pro Ser Val Val Asn Phe Phe Ala Ala Ile Thr Lys Met
                215                 220                 225
Lys Thr Cys Gly Tyr Gly Trp Trp
                230
```

<210> 66
<211> 102
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2672566CD1

<400> 66

```
Met Leu Ser Val Asp Met Glu Asn Lys Glu Asn Gly Ser Val Gly
 1               5                  10                  15
Val Lys Asn Ser Met Glu Asn Gly Arg Pro Pro Asp Pro Ala Asp
                20                  25                  30
Trp Ala Val Met Asp Val Val Asn Tyr Phe Arg Thr Val Gly Phe
                35                  40                  45
Glu Glu Gln Ala Ser Ala Phe Gln Glu Gln Glu Ile Asp Gly Lys
                50                  55                  60
Ser Leu Leu Leu Met Thr Arg Asn Asp Val Leu Thr Gly Leu Gln
                65                  70                  75
Leu Lys Leu Gly Pro Ala Leu Lys Ile Tyr Glu Tyr His Val Lys
                80                  85                  90
Pro Leu Gln Thr Lys His Leu Lys Asn Asn Ser Ser
                95                 100
```

<210> 67
<211> 287
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2689674CD1

<400> 67

```
Met Ala Ala Ser Leu Trp Met Gly Asp Leu Glu Pro Tyr Met Asp
 1               5                  10                  15
Glu Asn Phe Ile Ser Arg Ala Phe Ala Thr Met Gly Glu Thr Val
                20                  25                  30
Met Ser Val Lys Ile Ile Arg Asn Arg Leu Thr Gly Ile Pro Ala
                35                  40                  45
Gly Tyr Cys Phe Val Glu Phe Ala Asp Leu Ala Thr Ala Glu Lys
                50                  55                  60
Cys Leu His Lys Ile Asn Gly Lys Pro Leu Pro Gly Ala Thr Pro
                65                  70                  75
Ala Lys Arg Phe Lys Leu Asn Tyr Ala Thr Tyr Gly Lys Gln Pro
                80                  85                  90
Asp Asn Ser Pro Glu Tyr Ser Leu Phe Val Gly Asp Leu Thr Pro
                95                 100                 105
Asp Val Asp Asp Gly Met Leu Tyr Glu Phe Phe Val Lys Val Tyr
                110                 115                 120
Pro Ser Cys Arg Gly Gly Lys Val Val Leu Asp Gln Thr Gly Val
                125                 130                 135
```

Ser Lys Gly Tyr Gly Phe Val Lys Phe Thr Asp Glu Leu Glu Gln
140 145 150
Lys Arg Ala Leu Thr Glu Cys Gln Gly Ala Val Gly Leu Gly Ser
155 160 165
Lys Pro Val Arg Leu Ser Val Ala Ile Pro Lys Ala Ser Arg Val
170 175 180
Lys Pro Val Glu Tyr Ser Gln Met Tyr Ser Tyr Ser Tyr Asn Gln
185 190 195
Tyr Tyr Gln Gln Tyr Gln Asn Tyr Tyr Ala Gln Trp Gly Tyr Asp
200 205 210
Gln Asn Thr Gly Ser Tyr Ser Tyr Ser Tyr Pro Gln Tyr Gly Tyr
215 220 225
Thr Gln Ser Thr Met Gln Thr Tyr Glu Glu Val Gly Asp Asp Ala
230 235 240
Leu Glu Asp Pro Met Pro Gln Leu Asp Val Thr Glu Ala Asn Lys
245 250 255
Glu Phe Met Glu Gln Ser Glu Glu Leu Tyr Asp Ala Leu Met Asp
260 265 270
Cys His Trp Gln Pro Leu Asp Thr Val Ser Ser Glu Ile Pro Ala
275 280 285
Met Met

<210> 68
<211> 208
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2703282CD1

<400> 68
Met Lys Lys Asn Glu Val Tyr Glu Thr Phe Ser Tyr Pro Glu Ser
1 5 10 15
Tyr Ser Pro Thr Leu Pro Val Ser Arg Arg Glu Asn Asn Ser Pro
20 25 30
Ser Asn Leu Pro Arg Pro Ser Phe Cys Met Glu Glu Tyr Gln Arg
35 40 45
Ala Glu Leu Glu Glu Asp Pro Ile Leu Ser Arg Thr Pro Ser Pro
50 55 60
Val His Pro Ser Asp Phe Ser Glu His Asn Cys Gln Pro Tyr Tyr
65 70 75
Ala Ser Asp Gly Ala Thr Tyr Gly Ser Ser Ser Gly Leu Cys Leu
80 85 90
Gly Asn Pro Arg Ala Asp Ser Ile His Asn Thr Tyr Ser Thr Asp
95 100 105
His Ala Ser Ala Ala Pro Pro Ser Val Thr Arg Ser Pro Val Glu
110 115 120
Asn Asp Gly Tyr Ile Glu Glu Gly Ser Ile Thr Lys His Pro Ser
125 130 135
Thr Trp Ser Val Glu Ala Val Val Leu Phe Leu Lys Gln Thr Asp
140 145 150
Pro Leu Ala Leu Cys Pro Leu Val Asp Leu Phe Arg Ser His Glu
155 160 165
Ile Asp Gly Lys Ala Leu Leu Leu Leu Thr Ser Asp Val Leu Leu
170 175 180
Lys His Leu Gly Val Lys Leu Gly Thr Ala Val Lys Leu Cys Tyr
185 190 195
Tyr Ile Asp Arg Leu Lys Gln Gly Lys Cys Phe Glu Asn
200 205

<210> 69

<211> 177
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2738293CD1

<400> 69
Met Ser Lys Leu Ser Phe Arg Ala Arg Ala Leu Asp Ala Ala Lys
1 5 10 15
Pro Leu Pro Ile Tyr Arg Gly Lys Asp Met Pro Asp Leu Asn Asp
20 25 30
Cys Val Ser Ile Asn Arg Ala Val Pro Gln Met Pro Thr Gly Met
35 40 45
Glu Lys Glu Glu Glu Ser Glu His His Leu Gln Arg Ala Ile Ser
50 55 60
Ala Gln Gln Val Phe Arg Glu Lys Lys Glu Ser Met Val Ile Pro
65 70 75
Val Pro Glu Ala Glu Ser Asn Val Asn Tyr Tyr Asn Arg Leu Tyr
80 85 90
Lys Gly Glu Phe Lys Gln Pro Lys Gln Phe Ile His Ile Gln Arg
95 100 105
Ile Trp Gly His Tyr Gln Pro Glu Thr Thr Leu Lys Phe Leu Leu
110 115 120
Val Cys Phe Val His Leu Phe Leu Asp His Ser Ile Ser Phe Asn
125 130 135
Leu Gly Cys Arg Ser Ala Gln Gly Ser Val Leu Arg Lys Ile Phe
140 145 150
Cys Phe Ser Phe Leu Pro Lys Gly Lys Leu Arg Asn Thr Lys Phe
155 160 165
Phe Ala Phe Pro Phe Cys Met Ala Asn Leu Phe Leu
170 175

<210> 70
<211> 179
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2772776CD1

<400> 70
Met Ala Ala Thr Glu Pro Ile Leu Ala Ala Thr Gly Ser Pro Ala
1 5 10 15
Ala Val Pro Pro Glu Lys Leu Glu Gly Ala Gly Ser Ser Ser Ala
20 25 30
Pro Glu Arg Asn Cys Val Gly Ser Ser Leu Pro Glu Ala Ser Pro
35 40 45
Pro Ala Pro Glu Pro Ser Ser Pro Asn Ala Ala Val Pro Glu Ala
50 55 60
Ile Pro Thr Pro Arg Ala Ala Ala Ser Ala Ala Leu Glu Leu Pro
65 70 75
Leu Gly Pro Ala Pro Val Ser Val Ala Pro Gln Ala Glu Ala Glu
80 85 90
Ala Arg Ser Thr Pro Gly Pro Ala Gly Ser Arg Leu Gly Pro Glu
95 100 105
Thr Phe Arg Gln Arg Phe Arg Gln Phe Arg Tyr Gln Asp Ala Ala
110 115 120
Gly Pro Arg Glu Ala Phe Arg Gln Leu Arg Glu Leu Ser Arg Gln
125 130 135
Trp Leu Arg Pro Asp Ile Arg Thr Lys Glu Gln Ile Val Glu Met

```
                140                 145                 150
Leu Val Gln Glu Gln Leu Leu Ala Ile Leu Pro Glu Ala Ala Arg
                155                 160                 165
Ala Arg Arg Ile Arg Arg Arg Thr Asp Val Arg Ile Thr Gly
                170                 175
```

<210> 71
<211> 212
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2774476CD1

<400> 71

```
Met Asp Pro Ala Gly Ala Ala Asp Pro Ser Val Pro Pro Asn Pro
  1               5                  10                  15
Leu Thr His Leu Ser Leu Gln Asp Arg Ser Glu Met Gln Leu Gln
                 20                  25                  30
Ser Glu Ala Asp Arg Arg Ser Leu Pro Gly Thr Trp Thr Arg Ser
                 35                  40                  45
Ser Pro Glu His Thr Thr Ile Leu Arg Gly Gly Val Arg Arg Cys
                 50                  55                  60
Leu Gln Gln Gln Cys Glu Gln Thr Val Arg Ile Leu His Ala Lys
                 65                  70                  75
Val Ala Gln Lys Ser Tyr Gly Asn Glu Lys Arg Phe Phe Cys Pro
                 80                  85                  90
Pro Pro Cys Val Tyr Leu Ser Gly Pro Gly Trp Arg Val Lys Pro
                 95                 100                 105
Gly Gln Asp Gln Ala His Gln Ala Gly Glu Thr Gly Pro Thr Val
                110                 115                 120
Cys Gly Tyr Met Gly Leu Asp Ser Ala Ser Gly Ser Ala Thr Glu
                125                 130                 135
Thr Gln Lys Leu Asn Phe Glu Gln Gln Pro Asp Ser Arg Glu Phe
                140                 145                 150
Gly Cys Ala Lys Thr Leu Tyr Ile Ser Asp Ala Asp Lys Arg Lys
                155                 160                 165
His Phe Arg Leu Val Leu Arg Leu Val Leu Arg Gly Gly Arg Glu
                170                 175                 180
Leu Gly Thr Phe His Ser Arg Leu Ile Lys Val Ile Ser Lys Pro
                185                 190                 195
Ser Gln Lys Lys Gln Ser Leu Lys Asn Thr Asp Arg Glu Gln Gly
                200                 205                 210
Gly Ala
```

<210> 72
<211> 256
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2804624CD1

<400> 72

```
Met Lys Leu Leu Glu Asn Ser Ser Phe Glu Ala Ile Asn Ser Gln
  1               5                  10                  15
Leu Thr Val Glu Thr Gly Asp Ala His Ile Ile Gly Arg Ile Glu
                 20                  25                  30
Ser Tyr Ser Cys Lys Met Ala Gly Asp Asp Lys His Met Phe Lys
                 35                  40                  45
```

```
Gln Phe Cys Gln Glu Gly Gln Pro His Val Leu Glu Ala Leu Ser
                50                  55                  60
Pro Pro Gln Thr Ser Gly Leu Ser Pro Ser Arg Leu Ser Lys Ser
                65                  70                  75
Gln Gly Gly Glu Glu Glu Gly Pro Leu Ser Asp Lys Cys Ser Arg
                80                  85                  90
Lys Thr Leu Phe Tyr Leu Ile Ala Thr Leu Asn Glu Ser Phe Arg
                95                 100                 105
Pro Asp Tyr Asp Phe Ser Thr Ala Arg Ser His Glu Phe Ser Arg
               110                 115                 120
Glu Pro Ser Leu Ser Trp Val Val Asn Ala Val Asn Cys Ser Leu
               125                 130                 135
Phe Ser Ala Val Arg Glu Asp Phe Lys Asp Leu Lys Pro Gln Leu
               140                 145                 150
Trp Asn Ala Val Asp Glu Glu Ile Cys Leu Ala Glu Cys Asp Ile
               155                 160                 165
Tyr Ser Tyr Asn Pro Asp Leu Asp Ser Asp Pro Phe Gly Glu Asp
               170                 175                 180
Gly Ser Leu Trp Ser Phe Asn Tyr Phe Phe Tyr Asn Lys Arg Leu
               185                 190                 195
Lys Arg Ile Val Phe Phe Ser Cys Arg Ser Ile Ser Gly Ser Thr
               200                 205                 210
Tyr Thr Pro Ser Glu Ala Gly Asn Glu Leu Asp Met Glu Leu Gly
               215                 220                 225
Glu Glu Glu Val Glu Glu Glu Ser Arg Ser Arg Gly Ser Gly Ala
               230                 235                 240
Glu Glu Thr Ser Thr Met Glu Glu Asp Arg Val Pro Val Ile Cys
               245                 250                 255
Ile
```

<210> 73
<211> 475
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2848225CD1

<400> 73

```
Met Asp Ala Val Ala Phe Glu Asp Val Ala Val Asn Phe Thr Gln
  1               5                  10                  15
Glu Glu Trp Ala Leu Leu Gly Pro Ser Gln Lys Asn Leu Tyr Arg
                20                  25                  30
Tyr Val Met Gln Glu Thr Ile Arg Asn Leu Asp Cys Ile Arg Met
                35                  40                  45
Ile Trp Glu Glu Gln Asn Thr Glu Asp Gln Tyr Lys Asn Pro Arg
                50                  55                  60
Arg Asn Leu Arg Cys His Met Val Glu Arg Phe Ser Glu Ser Lys
                65                  70                  75
Asp Ser Ser Gln Cys Gly Glu Thr Phe Ser Leu Ile Arg Asp Ser
                80                  85                  90
Ile Val Asn Asn Ser Ile Cys Pro Gly Glu Asp Pro Cys Gln Ser
                95                 100                 105
Ala Glu Cys Glu Glu Val Ile Met Gly His Leu Ser Leu Asn Ser
               110                 115                 120
His Ile Arg Val Asp Ser Gly His Lys Pro His Glu Tyr Gln Glu
               125                 130                 135
Tyr Gly Glu Lys Pro His Thr His Lys Gln Arg Gly Lys Ala Phe
               140                 145                 150
Ser Tyr His His Ser Phe Gln Ser Arg Gly Arg Pro His Thr Gly
               155                 160                 165
```

Lys Lys Arg Tyr Glu Cys Lys Glu Cys Gly Lys Thr Phe Ser Ser
170 175 180
Arg Arg Asn Leu Arg Arg His Met Val Val Gln Gly Gly Asn Arg
185 190 195
Pro Tyr Lys Cys Lys Leu Cys Gly Lys Ala Phe Phe Trp Pro Ser
200 205 210
Leu Leu Arg Met His Glu Arg Thr His Thr Gly Glu Lys Pro Tyr
215 220 225
Glu Cys Lys Gln Cys Ser Lys Ala Phe Pro Phe Tyr Ser Ser Tyr
230 235 240
Arg Arg His Glu Arg Met His Thr Gly Glu Lys Pro Tyr Glu Cys
245 250 255
Lys Gln Cys Ser Lys Ala Leu Pro Asp Ser Ser Ser Tyr Ile Arg
260 265 270
His Glu Arg Thr His Thr Gly Glu Lys Pro Tyr Thr Cys Lys Gln
275 280 285
Cys Gly Lys Ala Phe Ser Val Ser Ser Ser Leu Arg Arg His Glu
290 295 300
Thr Thr His Ser Ala Glu Lys Pro Tyr Glu Cys Lys Gln Cys Gly
305 310 315
Lys Thr Phe His His Leu Gly Ser Phe Gln Ile His Met Lys Arg
320 325 330
His Thr Gly Asp Arg Pro His Lys Cys Lys Ile Cys Gly Lys Gly
335 340 345
Phe Asp Pro Ser Leu Val Arg Tyr His Glu Arg Ile His Thr Gly
350 355 360
Glu Lys Pro Tyr Glu Cys Lys Gln Cys Gly Lys Thr Leu Ser His
365 370 375
Ser Ser Ser Phe Arg Arg His Met Ile Met His Thr Gly Gly Gly
380 385 390
Pro His Lys Cys Lys Ile Cys Gly Lys Ala Phe Val Tyr Pro Ser
395 400 405
Val Cys Gln Arg His Glu Lys Ser His Ser Gly Glu Lys Pro Tyr
410 415 420
Glu Cys Lys Gln Cys Gly Lys Ala Leu Ser His Ser Ser Ser Phe
425 430 435
Arg Arg His Met Val Met His Thr Gly Asp Gly Pro Asn Lys Cys
440 445 450
Lys Val Cys Gly Lys Ala Phe Val Tyr Pro Ser Val Cys Gln Arg
455 460 465
His Glu Lys Thr His Trp Arg Glu Thr Ile
470 475

<210> 74
<211> 206
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2882241CD1

<400> 74
Met Glu Pro Leu Ala Ser Asn Ile Gln Val Leu Leu Gln Ala Ala
1 5 10 15
Glu Phe Leu Glu Arg Arg Glu Arg Glu Ala Glu His Gly Tyr Ala
20 25 30
Ser Leu Cys Pro His Arg Ser Pro Gly Pro Ile His Arg Arg Lys
35 40 45
Lys Arg Pro Pro Gln Ala Pro Gly Ala Gln Asp Ser Gly Arg Ser
50 55 60
Val His Asn Glu Leu Glu Lys Arg Arg Arg Ala Gln Leu Lys Arg
65 70 75

```
Cys Leu Glu Arg Leu Lys Gln Gln Met Pro Leu Gly Ala Asp Cys
                80                  85                  90
Ala Arg Tyr Thr Thr Leu Ser Leu Leu Arg Arg Ala Arg Met His
                95                  100                 105
Ile Gln Lys Leu Glu Asp Gln Glu Gln Arg Ala Arg Gln Leu Lys
                110                 115                 120
Glu Arg Leu Arg Ser Lys Gln Gln Ser Leu Gln Arg Gln Leu Glu
                125                 130                 135
Gln Leu Arg Gly Leu Ala Gly Ala Ala Glu Arg Glu Arg Leu Arg
                140                 145                 150
Ala Asp Ser Leu Asp Ser Ser Gly Leu Ser Ser Glu Arg Ser Asp
                155                 160                 165
Ser Asp Gln Glu Glu Leu Glu Val Asp Val Glu Ser Leu Val Phe
                170                 175                 180
Gly Gly Glu Ala Glu Leu Leu Arg Gly Phe Val Ala Gly Gln Glu
                185                 190                 195
His Ser Tyr Ser His Gly Gly Gly Ala Trp Leu
                200                 205
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<210> 75
<211> 596
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2939011CD1

<400> 75

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Met Arg Arg Asn Lys Gly Asp Ile Lys Glu Phe Trp Pro Gln Gln
 1               5                  10                  15
Ser Gln Leu Ser Asp Phe Met Lys Met Ala Asn Ala Glu Val Ser
                20                  25                  30
Val Pro Val Gly Asp Val Val Val Val Pro Thr Glu Gly Asn Glu
                35                  40                  45
Gly Glu Asn Pro Glu Asp Thr Lys Thr Gln Val Ile Leu Gln Leu
                50                  55                  60
Gln Pro Val Gln Gln Gly Leu Phe Ile Asp Gly His Phe Tyr Asn
                65                  70                  75
Arg Ile Tyr Glu Ala Gly Ser Glu Asn Asn Thr Ala Val Val Ala
                80                  85                  90
Val Glu Thr His Thr Ile His Lys Ile Glu Glu Gly Ile Asp Thr
                95                  100                 105
Gly Thr Ile Glu Ala Asn Glu Asp Met Glu Ile Ala Tyr Pro Ile
                110                 115                 120
Thr Cys Gly Glu Ser Lys Ala Ile Leu Leu Trp Lys Lys Phe Val
                125                 130                 135
Cys Pro Gly Ile Asn Val Lys Cys Val Lys Phe Asn Asp Gln Leu
                140                 145                 150
Ile Ser Pro Lys His Phe Val His Leu Ala Gly Lys Ser Thr Leu
                155                 160                 165
Lys Asp Trp Lys Arg Ala Ile Arg Leu Gly Gly Ile Met Leu Arg
                170                 175                 180
Lys Met Met Asp Ser Gly Gln Ile Asp Phe Tyr Gln His Asp Lys
                185                 190                 195
Val Cys Ser Asn Thr Cys Arg Ser Thr Lys Phe Asp Leu Leu Ile
                200                 205                 210
Ser Ser Ala Arg Ala Pro Val Pro Gly Gln Gln Thr Ser Val Val
                215                 220                 225
Gln Thr Pro Thr Ser Ala Asp Gly Ser Ile Thr Gln Ile Ala Ile
                230                 235                 240
Ser Glu Glu Ser Met Glu Glu Ala Gly Leu Glu Trp Asn Ser Ala
                245                 250                 255
```

Leu Thr Ala Ala Val Thr Met Ala Thr Glu Glu Gly Val Lys Lys
260 265 270
Asp Ser Glu Glu Ile Ser Glu Asp Thr Leu Met Phe Trp Lys Gly
275 280 285
Ile Ala Asp Val Gly Leu Met Glu Glu Val Val Cys Asn Ile Gln
290 295 300
Lys Glu Ile Glu Glu Leu Leu Arg Gly Val Gln Gln Arg Leu Ile
305 310 315
Gln Ala Pro Phe Gln Val Thr Asp Ala Ala Val Leu Asn Asn Val
320 325 330
Ala His Thr Phe Gly Leu Met Asp Thr Val Lys Lys Val Leu Asp
335 340 345
Asn Arg Arg Asn Gln Val Glu Gln Gly Glu Glu Gln Phe Leu Tyr
350 355 360
Thr Leu Thr Asp Leu Glu Arg Gln Leu Glu Glu Gln Lys Lys Gln
365 370 375
Gly Gln Asp His Arg Leu Lys Ser Gln Thr Val Gln Asn Val Val
380 385 390
Leu Met Pro Val Ser Thr Pro Lys Pro Pro Lys Arg Pro Arg Leu
395 400 405
Gln Arg Pro Ala Ser Thr Thr Val Leu Ser Pro Ser Pro Pro Val
410 415 420
Gln Gln Pro Gln Phe Thr Val Ile Ser Pro Ile Thr Ile Thr Pro
425 430 435
Val Gly Gln Ser Phe Ser Met Gly Asn Ile Pro Val Ala Thr Leu
440 445 450
Ser Gln Gly Ser Ser Pro Val Thr Val His Thr Leu Pro Ser Gly
455 460 465
Pro Gln Leu Phe Arg Tyr Ala Thr Val Val Ser Ser Ala Lys Ser
470 475 480
Ser Ser Pro Asp Thr Val Thr Ile His Pro Ser Ser Ser Leu Ala
485 490 495
Leu Leu Ser Ser Thr Ala Met Gln Asp Gly Ser Thr Leu Gly Asn
500 505 510
Met Thr Thr Met Val Ser Pro Val Glu Leu Val Ala Met Glu Ser
515 520 525
Gly Leu Thr Ser Ala Ile Gln Ala Val Glu Ser Thr Ser Glu Asp
530 535 540
Gly Gln Thr Ile Ile Glu Ile Asp Pro Ala Pro Asp Pro Glu Ala
545 550 555
Glu Asp Thr Glu Gly Lys Ala Val Ile Leu Glu Thr Glu Leu Arg
560 565 570
Thr Glu Glu Lys Val Val Ala Glu Met Glu Glu His Gln His Gln
575 580 585
Val His Asn Val Glu Ile Val Val Leu Glu Asp
590 595

<210> 76
<211> 644
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2947188CD1

<400> 76
Met Leu Glu Asn Tyr Gly Asn Val Ala Ser Leu Gly Phe Pro Leu
1 5 10 15
Leu Lys Pro Ala Val Ile Ser Gln Leu Glu Gly Gly Gly Glu Leu
20 25 30
Gly Gly Ser Ser Pro Leu Ala Ala Gly Thr Gly Leu Gln Gly Leu
35 40 45

Gln Thr Val Asp Ile Gln Thr Asp Asn Asp Leu Thr Lys Glu Met
50 55 60
Tyr Glu Gly Lys Glu Asn Val Ser Phe Glu Leu Gln Arg Asp Phe
65 70 75
Ser Gln Glu Thr Asp Phe Ser Glu Ala Ser Leu Leu Glu Lys Gln
80 85 90
Gln Glu Val His Ser Ala Gly Asn Ile Lys Lys Glu Lys Ser Asn
95 100 105
Thr Ile Asp Gly Thr Val Lys Asp Glu Thr Ser Pro Val Glu Glu
110 115 120
Cys Phe Phe Ser Gln Ser Ser Asn Ser Tyr Gln Cys His Thr Ile
125 130 135
Thr Gly Glu Gln Pro Ser Gly Cys Thr Gly Leu Gly Lys Ser Ile
140 145 150
Ser Phe Asp Thr Lys Leu Val Lys His Glu Ile Ile Asn Ser Glu
155 160 165
Glu Arg Pro Phe Lys Cys Glu Glu Leu Val Glu Pro Phe Arg Cys
170 175 180
Asp Ser Gln Leu Ile Gln His Gln Glu Asn Asn Thr Glu Glu Lys
185 190 195
Pro Tyr Gln Cys Ser Glu Cys Gly Lys Ala Phe Ser Ile Asn Glu
200 205 210
Lys Leu Ile Trp His Gln Arg Leu His Ser Gly Glu Lys Pro Phe
215 220 225
Lys Cys Val Glu Cys Gly Lys Ser Phe Ser Tyr Ser Ser His Tyr
230 235 240
Ile Thr His Gln Thr Ile His Ser Gly Glu Lys Pro Tyr Gln Cys
245 250 255
Lys Met Cys Gly Lys Ala Phe Ser Val Asn Gly Ser Leu Ser Arg
260 265 270
His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Gln Cys Lys Glu
275 280 285
Cys Gly Asn Gly Phe Ser Cys Ser Ser Ala Tyr Ile Thr His Gln
290 295 300
Arg Val His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Asp Cys Gly
305 310 315
Lys Ala Phe Asn Val Asn Ala Lys Leu Ile Gln His Gln Arg Ile
320 325 330
His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Glu Cys Gly Lys Gly
335 340 345
Phe Arg Cys Ser Ser Gln Leu Arg Gln His Gln Ser Ile His Thr
350 355 360
Gly Glu Lys Pro Tyr Gln Cys Lys Glu Cys Gly Lys Gly Phe Asn
365 370 375
Asn Asn Thr Lys Leu Ile Gln His Gln Arg Ile His Thr Gly Glu
380 385 390
Lys Pro Tyr Glu Cys Thr Glu Cys Gly Lys Ala Phe Ser Val Lys
395 400 405
Gly Lys Leu Ile Gln His Gln Arg Ile His Thr Gly Glu Lys Pro
410 415 420
Tyr Glu Cys Asn Glu Cys Gly Lys Ala Phe Arg Cys Asn Ser Gln
425 430 435
Phe Arg Gln His Leu Arg Ile His Thr Gly Glu Lys Pro Tyr Glu
440 445 450
Cys Asn Glu Cys Gly Lys Ala Phe Ser Val Asn Gly Lys Leu Met
455 460 465
Arg His Gln Arg Ile His Thr Gly Glu Lys Pro Phe Glu Cys Asn
470 475 480
Glu Cys Gly Arg Cys Phe Thr Ser Lys Arg Asn Leu Leu Asp His
485 490 495
His Arg Ile His Thr Gly Glu Lys Pro Tyr Gln Cys Lys Glu Cys
500 505 510
Gly Lys Ala Phe Ser Ile Asn Ala Lys Leu Thr Arg His Gln Arg

```
                515                     520                     525
Ile His Thr Gly Glu Lys Pro Phe Lys Cys Met Glu Cys Glu Lys
                530                     535                     540
Ala Phe Ser Cys Ser Ser Asn Tyr Ile Val His Gln Arg Ile His
                545                     550                     555
Thr Gly Glu Lys Pro Phe Gln Cys Lys Glu Cys Gly Lys Ala Phe
                560                     565                     570
His Val Asn Ala His Leu Ile Arg His Gln Arg Ser His Thr Gly
                575                     580                     585
Glu Lys Pro Phe Arg Cys Val Glu Cys Gly Lys Gly Phe Ser Phe
                590                     595                     600
Ser Ser Asp Tyr Ile Ile His Gln Thr Val His Thr Trp Lys Lys
                605                     610                     615
Pro Tyr Met Cys Ser Val Cys Gly Lys Ala Phe Arg Phe Ser Phe
                620                     625                     630
Gln Leu Ser Gln His Gln Ser Val His Ser Glu Gly Lys Ser
                635                     640

<210> 77
<211> 194
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3094001CD1

<400> 77
Met Pro Ser Ser Pro Leu Arg Val Ala Val Val Cys Ser Ser Asn
 1               5                  10                  15
Gln Asn Arg Ser Met Glu Ala His Asn Ile Leu Ser Lys Arg Gly
                20                  25                  30
Phe Ser Val Arg Ser Phe Gly Thr Gly Thr His Val Lys Leu Pro
                35                  40                  45
Gly Pro Ala Pro Asp Lys Pro Asn Val Tyr Asp Phe Lys Thr Thr
                50                  55                  60
Tyr Asp Gln Met Tyr Asn Asp Leu Leu Arg Lys Asp Lys Glu Leu
                65                  70                  75
Tyr Thr Gln Asn Gly Ile Leu His Met Leu Asp Arg Asn Lys Arg
                80                  85                  90
Ile Lys Pro Arg Pro Glu Arg Phe Gln Asn Cys Lys Asp Leu Phe
                95                 100                 105
Asp Leu Ile Leu Thr Cys Glu Glu Arg Val Tyr Asp Gln Val Val
                110                 115                 120
Glu Asp Leu Asn Ser Arg Glu Gln Glu Thr Cys Gln Pro Val His
                125                 130                 135
Val Val Asn Val Asp Ile Gln Asp Asn His Glu Glu Ala Thr Leu
                140                 145                 150
Gly Ala Phe Leu Ile Cys Glu Leu Cys Gln Cys Ile Gln His Thr
                155                 160                 165
Glu Asp Met Glu Asn Glu Ile Asp Glu Leu Leu Gln Glu Phe Glu
                170                 175                 180
Glu Lys Ser Gly Arg Thr Phe Leu His Thr Val Cys Phe Tyr
                185                 190

<210> 78
<211> 536
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3110061CD1
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<400> 78

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Met Ala Glu Met Asp Pro Thr Gln Gly Arg Val Val Phe Glu Asp
 1               5                  10                  15
Val Ala Ile Tyr Phe Ser Gln Glu Glu Trp Gly His Leu Asp Glu
                20                  25                  30
Ala Gln Arg Leu Leu Tyr Arg Asp Val Met Leu Glu Asn Leu Ala
                35                  40                  45
Leu Leu Ser Ser Leu Gly Ser Trp His Gly Ala Glu Asp Glu Glu
                50                  55                  60
Ala Pro Ser Gln Gln Gly Phe Ser Val Gly Val Ser Glu Val Thr
                65                  70                  75
Thr Ser Lys Pro Cys Leu Ser Ser Gln Lys Val His Pro Ser Glu
                80                  85                  90
Thr Cys Gly Pro Pro Leu Lys Asp Ile Leu Cys Leu Val Glu His
                95                 100                 105
Asn Gly Ile His Pro Glu Gln His Ile Tyr Ile Cys Glu Ala Glu
               110                 115                 120
Leu Phe Gln His Pro Lys Gln Gln Ile Gly Glu Asn Leu Ser Arg
               125                 130                 135
Gly Asp Asp Trp Ile Pro Ser Phe Gly Lys Asn His Arg Val His
               140                 145                 150
Met Ala Glu Glu Ile Phe Thr Cys Met Glu Gly Trp Lys Asp Leu
               155                 160                 165
Pro Ala Thr Ser Cys Leu Leu Gln His Gln Gly Pro Gln Ser Glu
               170                 175                 180
Trp Lys Pro Tyr Arg Asp Thr Glu Asp Arg Glu Ala Phe Gln Thr
               185                 190                 195
Gly Gln Asn Asp Tyr Lys Cys Ser Glu Cys Gly Lys Thr Phe Thr
               200                 205                 210
Cys Ser Tyr Ser Phe Val Glu His Gln Lys Ile His Thr Gly Glu
               215                 220                 225
Arg Ser Tyr Glu Cys Asn Lys Cys Gly Lys Phe Phe Lys Tyr Ser
               230                 235                 240
Ala Asn Phe Met Lys His Gln Thr Val His Thr Ser Glu Arg Thr
               245                 250                 255
Tyr Glu Cys Arg Glu Cys Gly Lys Ser Phe Met Tyr Asn Tyr Arg
               260                 265                 270
Leu Met Arg His Lys Arg Val His Thr Gly Glu Arg Pro Tyr Glu
               275                 280                 285
Cys Asn Thr Cys Gly Lys Phe Phe Arg Tyr Ser Ser Thr Phe Val
               290                 295                 300
Arg His Gln Arg Phe His Thr Gly Glu Arg Pro Tyr Glu Cys Arg
               305                 310                 315
Glu Cys Gly Lys Phe Phe Met Asp Ser Ser Thr Leu Ile Lys His
               320                 325                 330
Gln Arg Val His Thr Gly Glu Arg Pro Tyr Lys Cys Asn Asp Cys
               335                 340                 345
Gly Lys Phe Phe Arg Tyr Ile Ser Thr Leu Ile Arg His Gln Arg
               350                 355                 360
Ile His Thr Gly Glu Arg Pro Tyr Glu Cys Ser Val Cys Gly Glu
               365                 370                 375
Leu Phe Arg Tyr Asn Ser Ser Leu Val Lys His Trp Arg Asn His
               380                 385                 390
Thr Gly Glu Arg Pro Tyr Lys Cys Ser Glu Cys Gly Lys Ser Phe
               395                 400                 405
Arg Tyr His Cys Arg Leu Ile Arg His Gln Arg Val His Thr Gly
               410                 415                 420
Glu Arg Pro Tyr Glu Cys Ser Glu Cys Gly Lys Phe Phe Arg Tyr
               425                 430                 435
Asn Ser Asn Leu Ile Lys His Trp Arg Asn His Thr Gly Glu Arg
               440                 445                 450
Pro Tyr Glu Cys Arg Glu Cys Gly Lys Ala Phe Ser His Lys His
               455                 460                 465
```

Ile Leu Val Glu His Gln Lys Ile His Ser Gly Glu Arg Pro Tyr
470 475 480
Glu Cys Ser Glu Cys Gln Lys Ala Phe Ile Arg Lys Ser His Leu
485 490 495
Val His His Gln Lys Ile His Ser Glu Glu Arg Leu Val Cys Ser
500 505 510
Met Asn Val Gly Asn Ser Leu Ala Lys Thr Pro Thr Ser Leu Asn
515 520 525
Ile Arg Asp Phe Thr Met Glu Lys Val Tyr His
530 535

<210> 79
<211> 412
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3146614CD1

<400> 79
Met Ser Phe Val Ala Tyr Glu Glu Leu Ile Lys Glu Gly Asp Thr
1 5 10 15
Ala Ile Leu Ser Leu Gly His Gly Ala Met Val Ala Val Arg Val
20 25 30
Gln Arg Gly Ala Gln Thr Gln Thr Arg His Gly Val Leu Arg His
35 40 45
Ser Val Asp Leu Ile Gly Arg Pro Phe Gly Ser Lys Val Thr Cys
50 55 60
Gly Arg Gly Gly Trp Val Tyr Val Leu His Pro Thr Pro Glu Leu
65 70 75
Trp Thr Leu Asn Leu Pro His Arg Thr Gln Ile Leu Tyr Ser Thr
80 85 90
Asp Ile Ala Leu Ile Thr Met Met Leu Glu Leu Arg Pro Gly Ser
95 100 105
Val Val Cys Glu Ser Gly Thr Gly Ser Gly Ser Val Ser His Ala
110 115 120
Ile Ile Arg Thr Ile Ala Pro Thr Gly His Leu His Thr Val Glu
125 130 135
Phe His Gln Gln Arg Ala Glu Lys Ala Arg Glu Glu Phe Gln Glu
140 145 150
His Arg Val Gly Arg Trp Val Thr Val Arg Thr Gln Asp Val Cys
155 160 165
Arg Ser Gly Phe Gly Val Ser His Val Ala Asp Ala Val Phe Leu
170 175 180
Asp Ile Pro Ser Pro Trp Glu Ala Val Gly His Ala Trp Asp Ala
185 190 195
Leu Lys Val Glu Gly Gly Arg Phe Cys Ser Phe Ser Pro Cys Ile
200 205 210
Glu Gln Val Gln Arg Thr Cys Gln Ala Leu Ala Ala Arg Arg Leu
215 220 225
Leu Arg Ala Glu His Pro Gly Gly Ala Ala Thr Gly Leu Gln Arg
230 235 240
Ala His Cys Gln Pro Ala Thr Ala Arg Pro Gly His Arg His Arg
245 250 255
Trp Pro Cys Arg Leu Arg His Gln Pro Leu Pro Gln Arg His Ala
260 265 270
His Glu Gly Gly Arg Gly Pro His Arg Leu Pro Asp Leu Arg His
275 280 285
Gln Asp Pro Arg Leu Gly Gly Arg Leu Pro Gly His Gln Gly Ala
290 295 300
Gly Ser Thr Glu Gly Leu Gly Arg Glu Ala Arg Gly Thr Leu Tyr
305 310 315

Gly Gln Arg Cys Leu Pro Asp Thr Asp Gly Gly Val Gly Leu Gly
320 325 330
Gly Leu Leu Gly Gly Gln Ser Gly Thr Ala Gly Arg Ala Ala Val
335 340 345
Met Glu Glu Gln Cys Trp Gly Trp Ala Ser Ala Ile Pro Val Gln
350 355 360
Pro Cys Gly Pro Ser Gln Leu Leu Phe Val Ala Asn Met Lys Tyr
365 370 375
Pro Leu Pro Gln Ala Pro Leu Gly Val Glu Ala Lys Gly Cys Arg
380 385 390
Trp Gly Ser Leu Thr Pro Ser Gln Val Gly Leu Ser Arg Lys Gly
395 400 405
Val Glu Glu Gly Gly Gly His
410

<210> 80
<211> 482
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3295381CD1

<400> 80
Met Ala Lys Leu Tyr Glu Ala Val Thr Phe Lys Asp Val Ala Val
1 5 10 15
Ile Phe Thr Glu Glu Glu Leu Gly Leu Leu Asp Pro Ala Gln Arg
20 25 30
Lys Leu Tyr Arg Asp Val Met Leu Glu Asn Phe Arg Asn Leu Leu
35 40 45
Ser Val Gly His Gln Pro Phe His Gly Asp Thr Phe His Phe Leu
50 55 60
Arg Glu Glu Lys Phe Trp Val Met Gly Thr Thr Ser Gln Arg Glu
65 70 75
Gly Asn Leu Gly Gly Glu Ile Gln Thr Glu Met Glu Thr Val Pro
80 85 90
Glu Ala Gly Thr His Glu Glu Phe Ser Cys Lys Gln Ile Trp Glu
95 100 105
Gln Ile Ala Ser Asp Leu Thr Gly Ser Gln Asp Thr Thr Ile Ser
110 115 120
Asn Ser Gln Leu Phe Glu Gln Asp Asp Asn Pro Ser Gln Ile Lys
125 130 135
Ala Arg Leu Ser Thr Val His Thr Arg Glu Lys Pro Phe Gln Gly
140 145 150
Glu Asn Cys Lys Gln Phe Phe Ser Asp Val Ser Phe Phe Asp Leu
155 160 165
Pro Gln Gln Leu Tyr Ser Gly Glu Lys Ser His Thr Cys Asp Glu
170 175 180
Cys Gly Lys Ser Phe Cys Tyr Ile Ser Ala Leu His Ile His Gln
185 190 195
Arg Val His Met Gly Val Lys Cys Tyr Lys Cys Asp Val Cys Gly
200 205 210
Lys Glu Phe Ser Gln Ser Ser Arg Leu Gln Thr His Gln Arg Val
215 220 225
His Thr Gly Glu Lys Pro Phe Lys Cys Glu Gln Cys Gly Lys Gly
230 235 240
Phe Arg Cys Arg Ser Ala Leu Lys Val His Cys Lys Leu His Met
245 250 255
Arg Glu Lys Pro Tyr Asn Cys Glu Lys Cys Gly Lys Ala Phe Met
260 265 270
His Asn Phe Gln Leu Gln Lys His His Arg Ile His Thr Gly Glu
275 280 285

Lys Pro Phe Lys Cys Glu Ile Cys Gly Lys Ser Phe Cys Leu Arg
290 295 300
Ser Ser Leu Asn Arg His Cys Met Val His Thr Ala Glu Lys Leu
305 310 315
Tyr Lys Ser Glu Lys Tyr Gly Arg Gly Phe Ile Asp Arg Leu Asp
320 325 330
Leu His Lys His Gln Met Ile His Met Gly Gln Lys Pro Tyr Asn
335 340 345
Cys Lys Glu Cys Gly Lys Ser Phe Lys Trp Ser Ser Tyr Leu Leu
350 355 360
Val His Gln Arg Val His Thr Gly Glu Lys Pro Tyr Lys Cys Glu
365 370 375
Glu Cys Gly Lys Gly Tyr Ile Ser Lys Ser Gly Leu Asp Phe His
380 385 390
His Arg Thr His Thr Gly Glu Arg Ser Tyr Asn Cys Asp Asn Cys
395 400 405
Gly Lys Ser Phe Arg His Ala Ser Ser Ile Leu Asn His Lys Lys
410 415 420
Leu His Cys Gln Arg Lys Pro Leu Lys Cys Glu Asp Cys Gly Lys
425 430 435
Arg Leu Val Cys Arg Ser Tyr Cys Lys Asp Gln Gln Arg Asp His
440 445 450
Ser Gly Glu Asn Pro Ser Lys Cys Glu Asp Cys Gly Lys Arg Tyr
455 460 465
Lys Arg Arg Leu Asn Leu Asp Ile Ile Leu Ser Leu Phe Leu Asn
470 475 480
Asp Ile

<210> 81
<211> 554
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3364774CD1

<400> 81
Met Ser Ala Asp Gly Gly Gly Ile Gln Asp Thr Gln Asp Lys Glu
1 5 10 15
Thr Pro Pro Glu Val Pro Asp Arg Gly His Pro His Gln Glu Met
20 25 30
Pro Ser Lys Leu Gly Glu Ala Val Pro Ser Gly Asp Thr Gln Glu
35 40 45
Ser Leu His Ile Lys Met Glu Pro Glu Glu Pro His Ser Glu Gly
50 55 60
Ala Ser Gln Glu Asp Gly Ala Gln Gly Ala Trp Gly Trp Ala Pro
65 70 75
Leu Ser His Gly Ser Lys Glu Lys Ala Leu Phe Leu Pro Gly Gly
80 85 90
Ala Leu Pro Ser Pro Arg Ile Pro Val Leu Ser Arg Glu Gly Arg
95 100 105
Thr Arg Asp Arg Gln Met Ala Ala Ala Leu Leu Thr Ala Trp Ser
110 115 120
Gln Met Pro Val Thr Phe Glu Asp Val Ala Leu Tyr Leu Ser Arg
125 130 135
Glu Glu Trp Gly Arg Leu Asp His Thr Gln Gln Asn Phe Tyr Arg
140 145 150
Asp Val Leu Gln Lys Lys Asn Gly Leu Ser Leu Gly Phe Pro Phe
155 160 165
Ser Arg Pro Phe Trp Ala Pro Gln Ala His Gly Lys Gly Glu Ala
170 175 180

```
Ser Gly Ser Ser Arg Gln Ala Gly Asp Glu Lys Glu Trp Arg Gly
                185                 190                 195
Ala Cys Thr Gly Ala Val Glu Val Gly Gln Arg Val Gln Thr Ser
                200                 205                 210
Ser Val Ala Ala Leu Gly Asn Val Lys Pro Phe Arg Thr Arg Ala
                215                 220                 225
Gly Arg Val Gln Trp Gly Val Pro Gln Cys Ala Gln Glu Ala Ala
                230                 235                 240
Cys Gly Arg Ser Ser Gly Pro Ala Lys Asp Ser Gly Gln Pro Ala
                245                 250                 255
Glu Pro Asp Arg Thr Pro Asp Ala Ala Pro Pro Asp Pro Ser Pro
                260                 265                 270
Thr Glu Pro Gln Glu Tyr Arg Val Pro Glu Lys Pro Asn Glu Glu
                275                 280                 285
Glu Lys Gly Ala Pro Glu Ser Gly Glu Glu Gly Leu Ala Pro Asp
                290                 295                 300
Ser Glu Val Gly Arg Lys Ser Tyr Arg Cys Glu Gln Cys Gly Lys
                305                 310                 315
Gly Phe Ser Trp His Ser His Leu Val Thr His Arg Arg Thr His
                320                 325                 330
Thr Gly Glu Lys Pro Tyr Ala Cys Thr Asp Cys Gly Lys Arg Phe
                335                 340                 345
Gly Arg Ser Ser His Leu Ile Gln His Gln Ile Ile His Thr Gly
                350                 355                 360
Glu Lys Pro Tyr Thr Cys Pro Ala Cys Arg Lys Ser Phe Ser His
                365                 370                 375
His Ser Thr Leu Ile Gln His Gln Arg Ile His Thr Gly Glu Lys
                380                 385                 390
Pro Tyr Val Cys Asp Arg Cys Ala Lys Arg Phe Thr Arg Arg Ser
                395                 400                 405
Asp Leu Val Thr His Gln Gly Thr His Thr Gly Ala Lys Pro His
                410                 415                 420
Lys Cys Pro Ile Cys Ala Lys Cys Phe Thr Gln Ser Ser Ala Leu
                425                 430                 435
Val Thr His Gln Arg Thr His Thr Gly Val Lys Pro Tyr Pro Cys
                440                 445                 450
Pro Glu Cys Gly Lys Cys Phe Ser Gln Arg Ser Asn Leu Ile Ala
                455                 460                 465
His Asn Arg Thr His Thr Gly Glu Lys Pro Tyr His Cys Leu Asp
                470                 475                 480
Cys Gly Lys Ser Phe Ser His Ser Ser His Leu Thr Ala His Gln
                485                 490                 495
Arg Thr His Arg Gly Val Arg Pro Tyr Ala Cys Pro Leu Cys Gly
                500                 505                 510
Lys Ser Phe Ser Arg Arg Ser Asn Leu His Arg His Glu Lys Ile
                515                 520                 525
His Thr Thr Gly Pro Lys Ala Leu Ala Met Leu Met Leu Gly Ala
                530                 535                 540
Ala Ala Ala Gly Ala Leu Ala Thr Pro Pro Pro Ala Pro Thr
                545                 550
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<210> 82
<211> 488
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3397777CD1

<400> 82

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Met Ala Ser Lys Ile Leu Leu Asn Val Gln Glu Glu Val Thr Cys
  1               5                  10                  15
```

Pro Ile Cys Leu Glu Leu Leu Thr Glu Pro Leu Ser Leu Asp Cys
20 25 30
Gly His Ser Leu Cys Arg Ala Cys Ile Thr Val Ser Asn Lys Glu
35 40 45
Ala Val Thr Ser Met Gly Gly Lys Ser Ser Cys Pro Val Cys Gly
50 55 60
Ile Ser Tyr Ser Phe Glu His Leu Gln Ala Asn Gln His Leu Ala
65 70 75
Asn Ile Val Glu Arg Leu Lys Glu Val Lys Leu Ser Pro Asp Asn
80 85 90
Gly Lys Lys Arg Asp Leu Cys Asp His His Gly Glu Lys Leu Leu
95 100 105
Leu Phe Cys Lys Glu Asp Arg Lys Val Ile Cys Trp Leu Cys Glu
110 115 120
Arg Ser Gln Glu His Arg Gly His His Thr Val Leu Thr Glu Glu
125 130 135
Val Phe Lys Glu Cys Gln Glu Glu Leu Gln Ala Val Leu Lys Arg
140 145 150
Leu Lys Thr Glu Glu Glu Glu Ala Glu Lys Leu Glu Ala Asp Ile
155 160 165
Arg Glu Glu Lys Thr Ser Trp Lys Tyr Gln Val Gln Thr Glu Arg
170 175 180
Gln Arg Leu Gln Thr Glu Phe Asp Gln Leu Arg Ser Ile Leu Asn
185 190 195
Asn Glu Glu Gln Arg Glu Leu Gln Arg Leu Glu Glu Glu Glu Lys
200 205 210
Lys Thr Leu Asp Lys Phe Ala Glu Ala Glu Asp Glu Leu Val Gln
215 220 225
Gln Lys Gln Leu Val Arg Glu Leu Ile Ser Asp Val Glu Cys Arg
230 235 240
Ser Gln Trp Ser Thr Met Glu Leu Leu Gln Asp Met Ser Gly Ile
245 250 255
Met Lys Trp Ser Glu Ile Trp Arg Leu Lys Lys Pro Lys Met Val
260 265 270
Ser Lys Lys Leu Lys Thr Val Phe His Ala Pro Asp Leu Ser Arg
275 280 285
Met Leu Gln Met Phe Arg Glu Leu Thr Ala Val Arg Cys Tyr Trp
290 295 300
Val Asp Val Thr Leu Asn Ser Val Asn Leu Asn Leu Asn Leu Val
305 310 315
Leu Ser Glu Asp Gln Arg Gln Val Ile Ser Val Pro Ile Trp Pro
320 325 330
Phe Gln Trp Tyr Asn Tyr Gly Val Leu Gly Ser Gln Tyr Phe Ser
335 340 345
Ser Gly Lys His Tyr Trp Glu Val Asp Val Ser Lys Lys Thr Ala
350 355 360
Trp Ile Leu Gly Val Tyr Cys Arg Thr Tyr Ser Arg His Met Lys
365 370 375
Tyr Val Val Arg Arg Cys Ala Asn Arg Gln Asn Leu Tyr Thr Lys
380 385 390
Tyr Arg Pro Leu Phe Gly Tyr Trp Val Ile Gly Leu Gln Asn Lys
395 400 405
Cys Lys Tyr Gly Val Phe Glu Glu Ser Leu Ser Ser Asp Pro Glu
410 415 420
Val Leu Thr Leu Ser Met Ala Val Pro Pro Cys Arg Val Gly Val
425 430 435
Phe Leu Asp Tyr Glu Ala Gly Ile Val Ser Phe Phe Asn Val Thr
440 445 450
Ser His Gly Ser Leu Ile Tyr Lys Phe Ser Lys Cys Cys Phe Ser
455 460 465
Gln Pro Val Tyr Pro Tyr Phe Asn Pro Trp Asn Cys Pro Ala Pro
470 475 480
Met Thr Leu Cys Pro Pro Ser Ser

485

<210> 83
<211> 127
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3403046CD1

<400> 83
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Met Ser Gln Gly Leu Pro Ala Ala Gly Ser Ile Leu Gln Arg Ser
 1               5                  10                  15
Val Ala Ala Pro Gly Asn Gln Pro Gln Pro Gln Pro Gln Gln Gln
                20                  25                  30
Ser Pro Glu Asp Asp Asp Arg Lys Val Arg Arg Arg Glu Lys Asn
                35                  40                  45
Arg Val Ala Ala Gln Arg Ser Arg Lys Lys Gln Thr Gln Lys Ala
                50                  55                  60
Asp Lys Leu His Glu Glu Tyr Glu Ser Leu Glu Gln Glu Asn Thr
                65                  70                  75
Met Leu Arg Arg Glu Ile Gly Lys Leu Thr Glu Glu Leu Lys His
                80                  85                  90
Leu Thr Glu Ala Leu Lys Glu His Glu Lys Met Cys Pro Leu Leu
                95                 100                 105
Leu Cys Pro Met Asn Phe Val Pro Val Pro Pro Arg Pro Asp Pro
               110                 115                 120
Val Ala Gly Cys Leu Pro Arg
               125
```

<210> 84
<211> 532
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3538506CD1

<400> 84
```
Met Arg Cys Asp Phe Cys Gly Ala Gly Phe Asp Thr Arg Ala Gly
 1               5                  10                  15
Leu Ser Ser His Ala Arg Ala His Leu Arg Asp Phe Gly Ile Thr
                20                  25                  30
Asn Trp Glu Leu Thr Val Ser Pro Ile Asn Ile Leu Gln Glu Leu
                35                  40                  45
Leu Ala Thr Ser Ala Ala Glu Gln Pro Pro Ser Pro Leu Gly Arg
                50                  55                  60
Glu Pro Gly Gly Pro Pro Gly Ser Phe Leu Thr Ser Arg Arg Pro
                65                  70                  75
Arg Leu Pro Leu Thr Val Pro Phe Pro Pro Thr Trp Ala Glu Asp
                80                  85                  90
Pro Gly Pro Ala Tyr Gly Asp Ala Ser Gly Pro Glu Pro Ala Arg
                95                 100                 105
Asp Ile Arg Cys Glu Phe Cys Gly Glu Phe Phe Glu Asn Arg Lys
               110                 115                 120
Gly Leu Ser Ser His Ala Arg Ser His Leu Arg Gln Met Gly Val
               125                 130                 135
Thr Glu Trp Tyr Val Asn Gly Ser Pro Ile Asp Thr Leu Arg Glu
               140                 145                 150
Ile Leu Lys Arg Arg Thr Gln Ser Arg Pro Gly Gly Pro Pro Asn
               155                 160                 165
```

Pro Pro Gly Pro Ser Pro Lys Ala Leu Ala Lys Met Met Gly Gly
170 175 180
Ala Gly Pro Gly Ser Ser Leu Glu Ala Arg Ser Pro Ser Asp Leu
185 190 195
His Ile Ser Pro Leu Ala Lys Lys Leu Pro Pro Pro Pro Gly Ser
200 205 210
Pro Leu Gly His Ser Pro Thr Ala Ser Pro Pro Pro Thr Ala Arg
215 220 225
Lys Met Phe Pro Gly Leu Ala Ala Pro Ser Leu Pro Lys Lys Leu
230 235 240
Lys Pro Glu Gln Ile Arg Val Glu Ile Lys Arg Glu Met Leu Pro
245 250 255
Gly Ala Leu His Gly Glu Leu His Pro Ser Glu Gly Pro Trp Gly
260 265 270
Ala Pro Arg Glu Asp Met Thr Pro Leu Asn Leu Ser Ser Arg Ala
275 280 285
Glu Pro Val Arg Asp Ile Arg Cys Glu Phe Cys Gly Glu Phe Phe
290 295 300
Glu Asn Arg Lys Gly Leu Ser Ser His Ala Arg Ser His Leu Arg
305 310 315
Gln Met Gly Val Thr Glu Trp Ser Val Asn Gly Ser Pro Ile Asp
320 325 330
Thr Leu Arg Glu Ile Leu Lys Lys Lys Ser Lys Pro Cys Leu Ile
335 340 345
Lys Lys Glu Pro Pro Ala Gly Asp Leu Ala Pro Ala Leu Ala Glu
350 355 360
Asp Gly Pro Pro Thr Val Ala Pro Gly Pro Val Gln Ser Pro Leu
365 370 375
Pro Leu Ser Pro Leu Ala Gly Arg Pro Gly Lys Pro Gly Ala Gly
380 385 390
Pro Ala Gln Val Pro Arg Glu Leu Ser Leu Thr Pro Ile Thr Gly
395 400 405
Ala Lys Pro Ser Ala Thr Gly Tyr Leu Gly Ser Val Ala Ala Lys
410 415 420
Arg Pro Leu Gln Glu Asp Arg Leu Leu Pro Ala Glu Val Lys Ala
425 430 435
Lys Thr Tyr Ile Gln Thr Glu Leu Pro Phe Lys Ala Lys Thr Leu
440 445 450
His Glu Lys Thr Ser His Ser Ser Thr Glu Ala Cys Cys Glu Leu
455 460 465
Cys Gly Leu Tyr Phe Glu Asn Arg Lys Ala Leu Ala Ser His Ala
470 475 480
Arg Ala His Leu Arg Gln Phe Gly Val Thr Glu Trp Cys Val Asn
485 490 495
Gly Ser Pro Ile Glu Thr Leu Ser Glu Trp Ile Lys His Arg Pro
500 505 510
Gln Lys Val Gly Ala Tyr Arg Ser Tyr Ile Gln Gly Gly Arg Lys
515 520 525
Leu Ile Pro Phe Ser Glu Gly
530

<210> 85
<211> 353
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3575519CD1

<400> 85
Met Asp Tyr Lys Ser Ser Leu Ile Gln Asp Gly Asn Pro Met Glu
1 5 10 15

```
Asn Leu Glu Lys Gln Leu Ile Cys Pro Ile Cys Leu Glu Met Phe
                20                  25                  30
Thr Lys Pro Val Val Ile Leu Pro Cys Gln His Asn Leu Cys Arg
                35                  40                  45
Lys Cys Ala Asn Asp Ile Phe Gln Ala Ala Asn Pro Tyr Trp Thr
                50                  55                  60
Ser Arg Gly Ser Ser Val Ser Met Ser Gly Gly Arg Phe Arg Cys
                65                  70                  75
Pro Thr Cys Arg His Glu Val Ile Met Asp Arg His Gly Val Tyr
                80                  85                  90
Gly Leu Gln Arg Asn Leu Leu Val Glu Asn Ile Ile Asp Ile Tyr
                95                  100                 105
Lys Gln Glu Cys Ser Ser Arg Pro Leu Gln Lys Gly Ser His Pro
                110                 115                 120
Met Cys Lys Glu His Glu Asp Glu Lys Ile Asn Ile Tyr Cys Leu
                125                 130                 135
Thr Cys Glu Val Pro Thr Cys Ser Met Cys Lys Val Phe Gly Ile
                140                 145                 150
His Lys Ala Cys Glu Val Ala Pro Leu Gln Ser Val Phe Gln Gly
                155                 160                 165
Gln Lys Thr Glu Leu Asn Asn Cys Ile Ser Met Leu Val Ala Gly
                170                 175                 180
Asn Asp Arg Val Gln Thr Ile Ile Thr Gln Leu Glu Asp Ser Arg
                185                 190                 195
Arg Val Thr Lys Glu Asn Ser His Gln Val Lys Glu Glu Leu Ser
                200                 205                 210
Gln Lys Phe Asp Thr Leu Tyr Ala Ile Leu Asp Glu Lys Lys Ser
                215                 220                 225
Glu Leu Leu Gln Arg Ile Thr Gln Glu Gln Glu Lys Lys Leu Ser
                230                 235                 240
Phe Ile Glu Ala Leu Ile Gln Gln Tyr Gln Glu Gln Leu Asp Lys
                245                 250                 255
Ser Thr Lys Leu Val Glu Thr Ala Ile Gln Ser Leu Asp Glu Pro
                260                 265                 270
Gly Gly Ala Thr Phe Leu Leu Thr Ala Lys Gln Leu Ile Lys Ser
                275                 280                 285
Ile Val Glu Ala Ser Lys Gly Cys Gln Leu Gly Lys Thr Glu Gln
                290                 295                 300
Gly Phe Glu Asn Met Asp Phe Phe Thr Leu Asp Leu Glu His Ile
                305                 310                 315
Ala Asp Ala Leu Arg Ala Ile Asp Phe Gly Thr Asp Glu Glu Glu
                320                 325                 330
Glu Glu Phe Ile Glu Glu Glu Asp Gln Glu Glu Glu Glu Ser Thr
                335                 340                 345
Glu Gly Lys Glu Glu Gly His Gln
                350
```

```
<210> 86
<211> 407
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3598694CD1

<400> 86
Met Leu Ser Gln Ile Met Glu Asn Pro Leu Val Gln Asp Met Met
  1             5                   10                  15
Ser Asn Pro Asp Leu Met Arg His Met Ile Met Ala Asn Pro Gln
                20                  25                  30
Met Gln Gln Leu Met Glu Arg Asn Pro Glu Ile Ser His Met Leu
                35                  40                  45
```

Asn Asn Pro Glu Leu Met Arg Gln Thr Met Glu Leu Ala Arg Asn
50 55 60
Pro Ala Met Met Gln Glu Met Met Arg Asn Gln Asp Arg Ala Leu
65 70 75
Ser Asn Leu Glu Ser Ile Pro Gly Gly Tyr Asn Ala Leu Arg Arg
80 85 90
Met Tyr Thr Asp Ile Gln Glu Pro Met Phe Ser Ala Ala Arg Glu
95 100 105
Gln Phe Gly Asn Asn Pro Phe Ser Ser Leu Ala Gly Asn Ser Asp
110 115 120
Ser Ser Ser Ser Gln Pro Leu Arg Thr Glu Asn Arg Glu Pro Leu
125 130 135
Pro Asn Pro Trp Ser Pro Ser Pro Pro Thr Ser Gln Ala Pro Gly
140 145 150
Ser Gly Gly Glu Gly Thr Gly Gly Ser Gly Thr Ser Gln Val His
155 160 165
Pro Thr Val Ser Asn Pro Phe Gly Ile Asn Ala Ala Ser Leu Gly
170 175 180
Ser Gly Met Phe Asn Ser Pro Glu Met Gln Ala Leu Leu Gln Gln
185 190 195
Ile Ser Glu Asn Pro Gln Leu Met Gln Asn Val Ile Ser Ala Pro
200 205 210
Tyr Met Arg Ser Met Met Gln Thr Leu Ala Gln Asn Pro Asp Phe
215 220 225
Ala Ala Gln Met Met Val Asn Val Pro Leu Phe Ala Gly Asn Pro
230 235 240
Gln Leu Gln Glu Gln Leu Arg Leu Gln Leu Pro Val Phe Leu Gln
245 250 255
Gln Met Gln Asn Pro Glu Ser Leu Ser Ile Leu Thr Asn Pro Arg
260 265 270
Ala Met Gln Ala Leu Leu Gln Ile Gln Gln Gly Leu Gln Thr Leu
275 280 285
Gln Thr Glu Ala Pro Gly Leu Val Pro Ser Leu Gly Ser Phe Gly
290 295 300
Met Ser Arg Thr Pro Ala Pro Ser Ala Gly Ser Asn Ala Gly Ser
305 310 315
Thr Pro Glu Ala Pro Thr Ser Ser Pro Ala Thr Pro Ala Thr Ser
320 325 330
Ser Pro Thr Gly Ala Ser Ser Ala Gln Gln Gln Leu Met Gln Gln
335 340 345
Met Ile Gln Leu Leu Ala Gly Ser Gly Asn Ser Gln Val Gln Thr
350 355 360
Pro Glu Val Arg Phe Gln Gln Gln Leu Glu Gln Leu Asn Ser Met
365 370 375
Gly Phe Ile Asn Arg Glu Ala Asn Leu Gln Ala Leu Ile Ala Thr
380 385 390
Gly Gly Asp Ile Asn Ala Ala Ile Glu Arg Leu Leu Gly Ser Gln
395 400 405
Leu Ser

<210> 87
<211> 350
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3638819CD1

<220>
<221> unsure
<222> 301

<223> unknown or other

<400> 87
Met Leu Leu Asn Pro Glu Glu Lys Ser Pro Leu Asn Ile Ser Val
1   5   10   15
Gly Val His Pro Leu Asp Ser Phe Thr Gln Gly Phe Gly Glu Gln
                20   25   30
Pro Thr Gly Asp Leu Pro Ile Gly Pro Pro Phe Glu Met Pro Thr
                35   40   45
Gly Ala Leu Leu Ser Thr Pro Gln Phe Glu Met Leu Gln Asn Pro
                50   55   60
Leu Gly Leu Thr Gly Ala Leu Arg Gly Pro Gly Arg Arg Gly Gly
                65   70   75
Arg Ala Arg Gly Gly Gln Gly Pro Arg Pro Asn Ile Cys Gly Ile
                80   85   90
Cys Gly Lys Ser Phe Gly Arg Gly Ser Thr Pro Ile Gln His Gln
                95   100   105
Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Glu Val Cys Ser
                110   115   120
Lys Ala Phe Ser Gln Ser Ser Asp Leu Ile Lys His Gln Arg Thr
                125   130   135
His Thr Gly Glu Arg Pro Tyr Lys Cys Pro Arg Cys Gly Lys Ala
                140   145   150
Phe Ala Asp Ser Ser Tyr Leu Leu Arg His Gln Arg Thr His Ser
                155   160   165
Gly Gln Lys Pro Phe Lys Cys Pro His Cys Gly Lys Ala Phe Gly
                170   175   180
Asp Ser Ser Tyr Leu Leu Arg His Gln Arg Thr His Ser His Glu
                185   190   195
Arg Pro Tyr Ser Cys Thr Glu Cys Gly Lys Cys Tyr Ser Gln Asn
                200   205   210
Ser Ser Leu Arg Ser His Gln Arg Val His Thr Gly Gln Arg Pro
                215   220   225
Phe Ser Cys Gly Ile Cys Gly Lys Ser Phe Ser Gln Arg Ser Ala
                230   235   240
Leu Ile Pro His Ala Arg Ser His Ala Arg Glu Lys Pro Phe Lys
                245   250   255
Cys Leu Ser Cys Ala Asn Val Leu Ala Glu Leu Gly Ala Gly Asn
                260   265   270
Pro Arg Pro His Pro Leu Gly Gly Gly Arg Gly Trp Gly Gly Leu
                275   280   285
Cys Gly Gly Val Val Gly Trp Gly Gly Cys Gly Gly Glu Trp Gly
                290   295   300
Xaa Val Gly His Gly Val Gly Gly Val Leu Gly Val Val Gly Val
                305   310   315
Phe Cys Phe Phe Phe Ala Phe Trp Leu Phe Cys Phe Tyr Pro Phe
                320   325   330
Arg Trp Leu Phe Phe Pro Arg Asn Pro Phe Gly Ser Leu Ser Phe
                335   340   345
Trp Phe Pro Pro Val
                350

<210> 88
<211> 215
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3717139CD1

<400> 88
Met His Val Trp Pro Arg Trp Val Pro Pro Pro Val Ser Pro Glu

```
1               5                   10                  15
Leu Lys Asp Arg Lys Glu Asp Ala Lys Gly Met Glu Asp Glu Gly
                20                  25                  30
Gln Thr Lys Ile Lys Gln Arg Arg Ser Arg Thr Asn Phe Thr Leu
                35                  40                  45
Glu Gln Leu Asn Glu Leu Glu Arg Leu Phe Asp Glu Thr His Tyr
                50                  55                  60
Pro Asp Ala Phe Met Arg Glu Glu Leu Ser Gln Arg Leu Gly Leu
                65                  70                  75
Ser Glu Ala Arg Val Gln Val Trp Phe Gln Asn Arg Arg Ala Lys
                80                  85                  90
Cys Arg Lys Gln Glu Asn Gln Leu His Lys Gly Val Leu Ile Gly
                95                  100                 105
Ala Ala Ser Gln Phe Glu Ala Cys Arg Val Ala Pro Tyr Val Asn
                110                 115                 120
Val Gly Ala Leu Arg Met Pro Phe Gln Gln Val Gln Ala Gln Leu
                125                 130                 135
Gln Leu Asp Ser Ala Val Ala His Ala His His His Leu His Pro
                140                 145                 150
His Leu Ala Ala His Ala Pro Tyr Met Met Phe Pro Ala Pro Pro
                155                 160                 165
Phe Gly Leu Pro Leu Ala Thr Leu Ala Ala Asp Ser Ala Ser Ala
                170                 175                 180
Ala Ser Val Val Ala Ala Ala Ala Ala Ala Lys Thr Thr Ser Lys
                185                 190                 195
Asn Ser Ser Ile Ala Asp Leu Arg Leu Lys Ala Lys Lys His Ala
                200                 205                 210
Ala Ala Leu Gly Leu
                215

&lt;210&gt; 89
&lt;211&gt; 489
&lt;212&gt; PRT
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; misc_feature
&lt;223&gt; Incyte ID No: 3892962CD1

&lt;400&gt; 89
Met Lys Glu Leu Asp Pro Lys Asn Asp Ile Ser Glu Asp Lys Leu
1               5                   10                  15
Ser Val Val Gly Glu Ala Thr Gly Gly Pro Thr Arg Asn Gly Ala
                20                  25                  30
Arg Gly Pro Gly Ser Glu Gly Val Trp Glu Pro Gly Ser Trp Pro
                35                  40                  45
Glu Arg Pro Arg Gly Asp Ala Gly Ala Glu Trp Glu Pro Leu Gly
                50                  55                  60
Ile Pro Gln Gly Asn Lys Leu Leu Gly Gly Ser Val Pro Ala Cys
                65                  70                  75
His Glu Leu Lys Ala Phe Ala Asn Gln Gly Cys Val Leu Val Pro
                80                  85                  90
Pro Arg Leu Asp Asp Pro Thr Glu Lys Gly Ala Cys Pro Pro Val
                95                  100                 105
Arg Arg Gly Lys Asn Phe Ser Ser Thr Ser Asp Leu Ser Lys Pro
                110                 115                 120
Pro Met Pro Cys Glu Glu Lys Lys Thr Tyr Asp Cys Ser Glu Cys
                125                 130                 135
Gly Lys Ala Phe Ser Arg Ser Ser Ser Leu Ile Lys His Gln Arg
                140                 145                 150
Ile His Thr Gly Glu Lys Pro Phe Glu Cys Asp Thr Cys Gly Lys
                155                 160                 165
His Phe Ile Glu Arg Ser Ser Leu Thr Ile His Gln Arg Val His
```

170 175 180
Thr Gly Glu Lys Pro Tyr Ala Cys Gly Asp Cys Gly Lys Ala Phe
185 190 195
Ser Gln Arg Met Asn Leu Thr Val His Gln Arg Thr His Thr Gly
200 205 210
Glu Lys Pro Tyr Val Cys Asp Val Cys Gly Lys Ala Phe Arg Lys
215 220 225
Thr Ser Ser Leu Thr Gln His Glu Arg Ile His Thr Gly Glu Lys
230 235 240
Pro Tyr Ala Cys Gly Asp Cys Gly Lys Ala Phe Ser Gln Asn Met
245 250 255
His Leu Ile Val His Gln Arg Thr His Thr Gly Glu Lys Pro Tyr
260 265 270
Val Cys Pro Glu Cys Gly Arg Ala Phe Ser Gln Asn Met His Leu
275 280 285
Thr Glu His Gln Arg Thr His Thr Gly Glu Lys Pro Tyr Ala Cys
290 295 300
Lys Glu Cys Gly Lys Ala Phe Asn Lys Ser Ser Ser Leu Thr Leu
305 310 315
His Gln Arg Asn His Thr Gly Glu Lys Pro Tyr Val Cys Gly Glu
320 325 330
Cys Gly Lys Ala Phe Ser Gln Ser Ser Tyr Leu Ile Gln His Gln
335 340 345
Arg Phe His Ile Gly Val Lys Pro Phe Glu Cys Ser Glu Cys Gly
350 355 360
Lys Ala Phe Ser Lys Asn Ser Ser Leu Thr Gln His Gln Arg Ile
365 370 375
His Thr Gly Glu Lys Pro Tyr Glu Cys Tyr Ile Cys Lys Lys His
380 385 390
Phe Thr Gly Arg Ser Ser Leu Ile Val His Gln Ile Val His Thr
395 400 405
Gly Glu Lys Pro Tyr Val Cys Gly Glu Cys Gly Lys Ala Phe Ser
410 415 420
Gln Ser Ala Tyr Leu Ile Glu His Gln Arg Ile His Thr Gly Glu
425 430 435
Lys Pro Tyr Arg Cys Gly Gln Cys Gly Lys Ser Phe Ile Lys Asn
440 445 450
Ser Ser Leu Thr Val His Gln Arg Ile His Thr Gly Glu Lys Pro
455 460 465
Tyr Arg Cys Gly Glu Cys Gly Lys Thr Phe Ser Arg Asn Thr Asn
470 475 480
Leu Thr Arg His Leu Arg Ile His Thr
485

<210> 90
<211> 399
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4153521CD1

<400> 90
Met Ser Gln Val Thr Phe Ser Asp Val Ala Ile Asp Phe Ser His
1 5 10 15
Glu Glu Trp Ala Cys Leu Asp Ser Ala Gln Arg Asp Leu Tyr Lys
20 25 30
Asp Val Met Val Gln Asn Tyr Glu Asn Leu Val Ser Val Gly Leu
35 40 45
Ser Val Thr Lys Pro Tyr Val Ile Met Leu Leu Glu Asp Gly Lys
50 55 60
Glu Pro Trp Met Met Glu Lys Lys Leu Ser Lys Asp Trp Glu Ser

```
                    65                  70                  75
Arg Trp Glu Asn Lys Glu Leu Ser Thr Lys Lys Asp Ile Tyr Asp
                    80                  85                  90
Glu Asp Ser Pro Gln Pro Val Thr Met Glu Lys Val Val Lys Gln
                    95                  100                 105
Ser Tyr Glu Phe Ser Asn Ser Asn Lys Asn Leu Glu Tyr Thr Glu
                    110                 115                 120
Cys Asp Thr Phe Arg Ser Thr Phe His Ser Lys Ser Thr Leu Ser
                    125                 130                 135
Glu Pro Gln Asn Asn Ser Ala Glu Gly Asn Ser His Lys Tyr Asp
                    140                 145                 150
Ile Leu Lys Lys Asn Leu Ser Lys Lys Ser Val Ile Lys Ser Glu
                    155                 160                 165
Arg Ile Asn Gly Gly Lys Lys Leu Leu Asn Ser Asn Lys Ser Gly
                    170                 175                 180
Ala Ala Phe Asn Gln Ser Lys Ser Leu Thr Leu Pro Gln Thr Cys
                    185                 190                 195
Asn Arg Glu Lys Ile Tyr Thr Cys Ser Glu Cys Gly Lys Ala Phe
                    200                 205                 210
Gly Lys Gln Ser Ile Leu Ser Arg His Trp Arg Ile His Thr Gly
                    215                 220                 225
Glu Lys Pro Tyr Glu Cys Arg Glu Cys Gly Lys Thr Phe Ser His
                    230                 235                 240
Gly Ser Ser Leu Thr Arg His Gln Ile Ser His Ser Gly Glu Lys
                    245                 250                 255
Pro Tyr Lys Cys Ile Glu Cys Gly Lys Ala Phe Ser His Gly Ser
                    260                 265                 270
Ser Leu Thr Asn His Gln Ser Thr His Thr Gly Glu Lys Pro Tyr
                    275                 280                 285
Glu Cys Met Asn Cys Gly Lys Ser Phe Ser Arg Val Ser Leu Leu
                    290                 295                 300
Ile Gln His Leu Arg Ile His Thr Gln Glu Lys Arg Tyr Glu Cys
                    305                 310                 315
Arg Ile Cys Gly Lys Ala Phe Ile His Ser Ser Ser Leu Ile His
                    320                 325                 330
His Gln Lys Ser His Thr Gly Glu Lys Pro Tyr Glu Cys Arg Glu
                    335                 340                 345
Cys Gly Lys Ala Phe Cys Cys Ser Ser His Leu Thr Gln His Gln
                    350                 355                 360
Arg Ile His Ser Met Lys Lys Lys Tyr Glu Cys Asn Lys Cys Leu
                    365                 370                 375
Lys Val Phe Ser Ser Phe Ser Phe Leu Val Gln His Gln Ser Ile
                    380                 385                 390
His Thr Glu Glu Lys Pro Phe Glu Val
                    395

<210> 91
<211> 309
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4585038CD1

<400> 91
Met Ala Pro Asn Leu Asp Ser Phe Gly Arg Asp Arg Ala Leu Tyr
1                   5                   10                  15
Gln Glu His Ala Lys Arg Arg Ile Ala Glu Arg Glu Ala Arg Arg
                    20                  25                  30
Thr Arg Arg Arg Gln Ala Arg Glu Gln Thr Gly Lys Met Ala Asp
                    35                  40                  45
His Leu Glu Gly Leu Ser Ser Asp Asp Glu Glu Thr Ser Thr Asp
```

```
                    50                       55                      60
Ile Thr Asn Phe Asn Leu Glu Lys Asp Arg Ile Ser Lys Glu Ser
                    65                       70                      75
Gly Lys Val Phe Glu Asp Val Leu Glu Ser Phe Tyr Ser Ile Asp
                    80                       85                      90
Cys Ile Lys Ser Gln Phe Glu Ala Trp Arg Ser Lys Tyr Tyr Thr
                    95                       100                     105
Ser Tyr Lys Asp Ala Tyr Ile Gly Leu Cys Leu Pro Lys Leu Phe
                    110                      115                     120
Asn Pro Leu Ile Arg Leu Gln Leu Leu Thr Trp Thr Pro Leu Glu
                    125                      130                     135
Ala Lys Cys Arg Asp Phe Glu Asn Met Leu Trp Phe Glu Ser Leu
                    140                      145                     150
Leu Phe Tyr Gly Cys Glu Glu Arg Glu Gln Glu Lys Asp Asp Val
                    155                      160                     165
Asp Val Ala Leu Leu Pro Thr Ile Val Glu Lys Val Ile Leu Pro
                    170                      175                     180
Lys Leu Thr Val Ile Ala Glu Asn Met Trp Asp Pro Phe Ser Thr
                    185                      190                     195
Thr Gln Thr Ser Arg Met Val Gly Ile Thr Leu Lys Leu Ile Asn
                    200                      205                     210
Gly Tyr Pro Ser Val Val Asn Ala Glu Asn Lys Asn Thr Gln Val
                    215                      220                     225
Tyr Leu Lys Ala Leu Leu Leu Arg Met Arg Arg Thr Leu Asp Asp
                    230                      235                     240
Asp Val Phe Met Pro Leu Tyr Pro Lys Asn Val Leu Glu Asn Lys
                    245                      250                     255
Asn Ser Gly Pro Tyr Leu Phe Phe Gln Arg Gln Phe Trp Ser Ser
                    260                      265                     270
Val Lys Val Ile Lys Pro Pro Phe Gln Arg Gly Ser Cys Pro Ile
                    275                      280                     285
Pro Arg Arg Lys Glu Cys Cys Ser Glu Arg Pro Arg Arg Ile Trp
                    290                      295                     300
Thr Asp Arg Pro Cys Val Val Phe Ser
                    305
```

<210> 92
<211> 361
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4674640CD1

<400> 92

```
Met Ala Leu Asn Val Ala Pro Val Arg Asp Thr Lys Trp Leu Thr
  1                 5                        10                      15
Leu Glu Val Cys Arg Gln Phe Gln Arg Gly Thr Cys Ser Arg Ser
                    20                       25                      30
Asp Glu Glu Cys Lys Phe Ala His Pro Pro Lys Ser Cys Gln Val
                    35                       40                      45
Glu Asn Gly Arg Val Ile Ala Cys Phe Asp Ser Leu Lys Gly Arg
                    50                       55                      60
Cys Ser Arg Glu Asn Cys Lys Tyr Leu His Pro Pro Thr His Leu
                    65                       70                      75
Lys Thr Gln Leu Glu Ile Asn Gly Arg Asn Asn Leu Ile Gln Gln
                    80                       85                      90
Lys Thr Ala Ala Ala Met Leu Ala Gln Gln Met Gln Phe Met Phe
                    95                       100                     105
Pro Gly Thr Pro Leu His Pro Val Pro Thr Phe Pro Val Gly Pro
                    110                      115                     120
Ala Ile Gly Thr Asn Thr Ala Ile Ser Phe Ala Pro Tyr Leu Ala
```

```
                125                 130                 135
Pro Val Thr Pro Gly Val Gly Leu Val Pro Thr Glu Ile Leu Pro
                140                 145                 150
Thr Thr Pro Val Ile Val Pro Gly Ser Pro Pro Val Thr Val Pro
                155                 160                 165
Gly Ser Thr Ala Thr Gln Lys Leu Leu Arg Thr Asp Lys Leu Glu
                170                 175                 180
Val Cys Arg Glu Phe Gln Arg Gly Asn Cys Ala Arg Gly Glu Thr
                185                 190                 195
Asp Cys Arg Phe Ala His Pro Ala Asp Ser Thr Met Ile Asp Thr
                200                 205                 210
Ser Asp Asn Thr Val Thr Val Cys Met Asp Tyr Ile Lys Gly Arg
                215                 220                 225
Cys Met Arg Glu Lys Cys Lys Tyr Phe His Pro Pro Ala His Leu
                230                 235                 240
Gln Ala Lys Ile Lys Ala Ala Gln His Gln Ala Asn Gln Ala Ala
                245                 250                 255
Val Ala Ala Gln Ala Ala Ala Ala Ala Ala Thr Val Met Ala Phe
                260                 265                 270
Pro Pro Gly Ala Leu His Pro Leu Pro Lys Arg Gln Ala Leu Glu
                275                 280                 285
Lys Ser Asn Gly Thr Ser Ala Val Phe Asn Pro Ser Val Leu His
                290                 295                 300
Tyr Gln Gln Ala Leu Thr Ser Ala Gln Leu Gln Gln His Ala Ala
                305                 310                 315
Phe Ile Pro Thr Asp Asn Ser Glu Ile Ile Ser Arg Asn Gly Met
                320                 325                 330
Glu Cys Gln Glu Ser Ala Leu Arg Ile Thr Lys His Cys Tyr Cys
                335                 340                 345
Thr Tyr Tyr Pro Val Ser Ser Ser Ile Glu Leu Pro Gln Thr Ala
                350                 355                 360
Cys


<210> 93
<211> 540
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4676066CD1

<400> 93
Met Pro Pro Cys Ala Val Thr Pro Pro Pro Pro Thr Ser Gln Pro
 1               5                  10                  15
Asn Trp Leu Thr Leu Cys Leu Phe Pro Ala Gly Gly Ser Ser Gln
                20                  25                  30
Ile His Leu Ser Asn Thr Glu Thr Ser Gly Arg Pro Cys Thr Arg
                35                  40                  45
Pro Pro Val Arg Asp Pro Arg Gln Thr Pro Ser Gln Pro Ala Arg
                50                  55                  60
Pro Pro Gly Val Gln Glu Arg His Gln Pro Gly Leu Gln Ala Pro
                65                  70                  75
Leu Ala Tyr Tyr Gly Thr Ser Trp Pro Leu Gln Ser His Leu Met
                80                  85                  90
His Arg Tyr His Ser Pro Val Thr Pro Phe Ser Pro Leu Gln Gly
                95                 100                 105
Leu Gly Pro Glu Cys Arg Ser Val Ala Ser Ala Arg Pro His Thr
               110                 115                 120
His Gly Gly Cys Cys Pro Gln Ala Glu Gln Ser Lys Val Leu Ser
               125                 130                 135
Ala Val Glu Asp Arg Met Asp Glu Leu Gly Ala Gly Ile Ala Gln
```

140 145 150
Ser Arg Arg Thr Val Ala Leu Ile Lys Ser Ala Ala Val Ala Glu
155 160 165
Arg Glu Arg Val Ser Arg Leu Phe Ala Asp Ala Ala Ala Ala Leu
170 175 180
Gln Gly Phe Gln Thr Gln Val Leu Gly Phe Ile Glu Glu Gly Glu
185 190 195
Ala Ala Met Leu Gly Arg Ser Gln Gly Asp Leu Arg Arg Gln Glu
200 205 210
Glu Gln Arg Ser Arg Leu Ser Arg Ala Arg Gln Asn Leu Ser Gln
215 220 225
Val Pro Glu Ala Asp Ser Val Ser Phe Leu Gln Glu Leu Leu Ala
230 235 240
Leu Arg Leu Ala Leu Glu Asp Gly Cys Gly Pro Gly Pro Gly Pro
245 250 255
Pro Arg Glu Leu Ser Phe Thr Lys Ser Ser Gln Ala Val Arg Ala
260 265 270
Val Arg Asp Met Leu Ala Val Ala Cys Val Asn Gln Trp Glu Gln
275 280 285
Leu Arg Gly Pro Gly Gly Asn Glu Asp Gly Pro Gln Lys Leu Asp
290 295 300
Ser Glu Ala Asp Ala Glu Pro Gln Asp Leu Glu Ser Thr Asn Leu
305 310 315
Leu Glu Ser Glu Ala Pro Arg Asp Tyr Phe Leu Lys Phe Ala Tyr
320 325 330
Ile Val Asp Leu Asp Ser Asp Thr Ala Asp Lys Phe Leu Gln Leu
335 340 345
Phe Gly Thr Lys Gly Val Lys Arg Val Leu Cys Pro Ile Asn Tyr
350 355 360
Pro Leu Ser Pro Thr Arg Phe Thr His Cys Glu Gln Val Leu Gly
365 370 375
Glu Gly Ala Leu Asp Arg Gly Thr Tyr Tyr Trp Glu Val Glu Ile
380 385 390
Ile Glu Gly Trp Val Ser Met Gly Val Met Ala Glu Asp Phe Ser
395 400 405
Pro Gln Glu Pro Tyr Asp Arg Gly Arg Leu Gly Arg Asn Ala His
410 415 420
Ser Cys Cys Leu Gln Trp Asn Gly Arg Ser Phe Ser Val Trp Phe
425 430 435
His Gly Leu Glu Ala Pro Leu Pro His Pro Phe Ser Pro Thr Val
440 445 450
Gly Val Cys Leu Glu Tyr Ala Asp Arg Ala Leu Ala Phe Tyr Ala
455 460 465
Val Arg Asp Gly Lys Met Ser Leu Leu Arg Arg Leu Lys Ala Ser
470 475 480
Arg Pro Arg Arg Gly Gly Ile Pro Ala Ser Pro Ile Asp Pro Phe
485 490 495
Gln Ser Arg Leu Asp Ser His Phe Ala Gly Leu Phe Thr His Arg
500 505 510
Leu Lys Pro Ala Phe Phe Leu Glu Ser Val Asp Ala His Leu Gln
515 520 525
Ile Gly Pro Leu Lys Lys Ser Cys Ile Ser Val Leu Lys Arg Arg
530 535 540

<210> 94
<211> 84
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4830687CD1

```
<400> 94
Met Lys Val Lys Ile Lys Cys Trp Asn Gly Val Ala Thr Trp Leu
 1               5                  10                  15
Trp Val Ala Asn Asp Glu Asn Cys Gly Ile Cys Arg Met Ala Phe
                20                  25                  30
Asn Gly Cys Cys Pro Asp Cys Lys Val Pro Gly Asp Asp Cys Pro
                35                  40                  45
Leu Val Trp Gly Gln Cys Ser His Cys Phe His Met His Cys Ile
                50                  55                  60
Leu Lys Trp Leu His Ala Gln Gln Val Gln Gln His Cys Pro Met
                65                  70                  75
Cys Arg Gln Glu Trp Lys Phe Lys Glu
                80

<210> 95
<211> 1312
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4880891CD1

<400> 95
Met Lys Ala Leu Asp Glu Pro Pro Tyr Leu Thr Val Gly Thr Asp
 1               5                  10                  15
Val Ser Ala Lys Tyr Arg Gly Ala Phe Cys Glu Ala Lys Ile Lys
                20                  25                  30
Thr Ala Lys Arg Leu Val Lys Val Lys Val Thr Phe Arg His Asp
                35                  40                  45
Ser Ser Thr Val Glu Val Gln Asp Asp His Ile Lys Gly Pro Leu
                50                  55                  60
Lys Val Gly Ala Ile Val Glu Val Lys Asn Leu Asp Gly Ala Tyr
                65                  70                  75
Gln Glu Ala Val Ile Asn Lys Leu Thr Asp Ala Ser Trp Tyr Thr
                80                  85                  90
Val Val Phe Asp Asp Gly Asp Glu Lys Thr Leu Arg Arg Ser Ser
                95                 100                 105
Leu Cys Leu Lys Gly Glu Arg His Phe Ala Glu Ser Glu Thr Leu
               110                 115                 120
Asp Gln Leu Pro Leu Thr Asn Pro Glu His Phe Gly Thr Pro Val
               125                 130                 135
Ile Gly Lys Lys Thr Asn Arg Gly Arg Arg Ser Asn His Ile Pro
               140                 145                 150
Glu Glu Glu Ser Ser Ser Ser Ser Ser Asp Glu Asp Glu Asp Asp
               155                 160                 165
Arg Lys Gln Ile Asp Glu Leu Leu Gly Lys Val Val Cys Val Asp
               170                 175                 180
Tyr Ile Ser Leu Asp Lys Lys Lys Ala Leu Trp Phe Pro Ala Leu
               185                 190                 195
Val Val Cys Pro Asp Cys Ser Asp Glu Ile Ala Val Lys Lys Asp
               200                 205                 210
Asn Ile Leu Val Arg Ser Phe Lys Asp Gly Lys Phe Thr Ser Val
               215                 220                 225
Pro Arg Lys Asp Val His Glu Ile Thr Ser Asp Thr Ala Pro Lys
               230                 235                 240
Pro Asp Ala Val Leu Lys Gln Ala Phe Glu Gln Ala Leu Glu Phe
               245                 250                 255
His Lys Ser Arg Thr Ile Pro Ala Asn Trp Lys Thr Glu Leu Lys
               260                 265                 270
Glu Asp Ser Ser Ser Ser Glu Ala Glu Glu Glu Glu Glu Glu Glu
               275                 280                 285
Asp Asp Glu Lys Glu Lys Glu Asp Asn Ser Ser Glu Glu Glu Glu
```

290 295 300
Glu Ile Glu Pro Phe Pro Glu Glu Arg Glu Asn Phe Leu Gln Gln
305 310 315
Leu Tyr Lys Phe Met Glu Asp Arg Gly Thr Pro Ile Asn Lys Arg
320 325 330
Pro Val Leu Gly Tyr Arg Asn Leu Asn Leu Phe Lys Leu Phe Arg
335 340 345
Leu Val His Lys Leu Gly Gly Phe Asp Asn Ile Glu Ser Gly Ala
350 355 360
Val Trp Lys Gln Val Tyr Gln Asp Leu Gly Ile Pro Val Leu Asn
365 370 375
Ser Ala Ala Gly Tyr Asn Val Lys Cys Ala Tyr Lys Lys Tyr Leu
380 385 390
Tyr Gly Phe Glu Glu Tyr Cys Arg Ser Ala Asn Ile Glu Phe Gln
395 400 405
Met Ala Leu Pro Glu Lys Val Val Asn Lys Gln Cys Lys Glu Cys
410 415 420
Glu Asn Val Lys Glu Ile Lys Val Lys Glu Glu Asn Glu Thr Glu
425 430 435
Ile Lys Glu Ile Lys Met Glu Glu Glu Arg Asn Ile Ile Pro Arg
440 445 450
Glu Glu Lys Pro Ile Glu Asp Glu Ile Glu Arg Lys Glu Asn Ile
455 460 465
Lys Pro Ser Leu Gly Ser Lys Lys Asn Leu Leu Glu Ser Ile Pro
470 475 480
Thr His Ser Asp Gln Glu Lys Glu Val Asn Ile Lys Lys Pro Glu
485 490 495
Asp Asn Glu Asn Leu Asp Asp Lys Asp Asp Asp Thr Thr Arg Val
500 505 510
Asp Glu Ser Leu Asn Ile Lys Val Glu Ala Glu Glu Glu Lys Ala
515 520 525
Lys Ser Gly Asp Glu Thr Asn Lys Glu Glu Asp Glu Asp Asp Glu
530 535 540
Glu Ala Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Asp Glu
545 550 555
Asp Asp Asp Asp Asn Asn Glu Glu Glu Glu Phe Glu Cys Tyr Pro
560 565 570
Pro Gly Met Lys Val Gln Val Arg Tyr Gly Arg Gly Lys Asn Gln
575 580 585
Lys Met Tyr Glu Ala Ser Ile Lys Asp Ser Asp Val Glu Gly Gly
590 595 600
Glu Val Leu Tyr Leu Val His Tyr Cys Gly Trp Asn Val Arg Tyr
605 610 615
Asp Glu Trp Ile Lys Ala Asp Lys Ile Val Arg Pro Ala Asp Lys
620 625 630
Asn Val Pro Lys Ile Lys His Arg Lys Lys Ile Lys Asn Lys Leu
635 640 645
Asp Lys Glu Lys Asp Lys Asp Glu Lys Tyr Ser Pro Lys Asn Cys
650 655 660
Lys Leu Arg Arg Leu Ser Lys Pro Pro Phe Gln Thr Asn Pro Ser
665 670 675
Pro Glu Met Val Ser Lys Leu Asp Leu Thr Asp Ala Lys Asn Ser
680 685 690
Asp Thr Ala His Ile Lys Ser Ile Glu Ile Thr Ser Ile Leu Asn
695 700 705
Gly Leu Gln Ala Ser Glu Ser Ser Ala Glu Asp Ser Glu Gln Glu
710 715 720
Asp Glu Arg Gly Ala Gln Asp Met Asp Asn Asn Gly Lys Glu Glu
725 730 735
Ser Lys Ile Asp His Leu Thr Asn Asn Arg Asn Asp Leu Ile Ser
740 745 750
Lys Glu Glu Gln Asn Ser Ser Ser Leu Leu Glu Glu Asn Lys Val
755 760 765

His Ala Asp Leu Val Ile Ser Lys Pro Val Ser Lys Ser Pro Glu
770 775 780
Arg Leu Arg Lys Asp Ile Glu Val Leu Ser Glu Asp Thr Asp Tyr
785 790 795
Glu Glu Asp Glu Val Thr Lys Lys Arg Lys Asp Val Lys Lys Asp
800 805 810
Thr Thr Asp Lys Ser Ser Lys Pro Gln Ile Lys Arg Gly Lys Arg
815 820 825
Arg Tyr Cys Asn Thr Glu Glu Cys Leu Lys Thr Gly Ser Pro Gly
830 835 840
Lys Lys Glu Glu Lys Ala Lys Asn Lys Glu Ser Leu Cys Met Glu
845 850 855
Asn Ser Ser Asn Ser Ser Ser Asp Glu Asp Glu Glu Glu Thr Lys
860 865 870
Ala Lys Met Thr Pro Thr Lys Lys Tyr Asn Gly Leu Glu Glu Lys
875 880 885
Arg Lys Ser Leu Arg Thr Thr Gly Phe Tyr Ser Gly Phe Ser Glu
890 895 900
Val Ala Glu Lys Arg Ile Lys Leu Leu Asn Asn Ser Asp Glu Arg
905 910 915
Leu Gln Asn Ser Arg Ala Lys Asp Arg Lys Asp Val Trp Ser Ser
920 925 930
Ile Gln Gly Gln Trp Pro Lys Lys Thr Leu Lys Glu Leu Phe Ser
935 940 945
Asp Ser Asp Thr Glu Ala Ala Ala Ser Pro Pro His Pro Ala Pro
950 955 960
Glu Glu Gly Val Ala Glu Glu Ser Leu Gln Thr Val Ala Glu Glu
965 970 975
Glu Ser Cys Ser Pro Ser Val Glu Leu Glu Lys Pro Pro Pro Val
980 985 990
Asn Val Asp Ser Lys Pro Ile Glu Glu Lys Thr Val Glu Val Asn
995 1000 1005
Asp Arg Lys Ala Glu Phe Pro Ser Ser Gly Ser Asn Ser Val Leu
1010 1015 1020
Asn Thr Pro Pro Thr Thr Pro Glu Ser Pro Ser Ser Val Thr Val
1025 1030 1035
Thr Glu Gly Ser Arg Gln Gln Ser Ser Val Thr Val Ser Glu Pro
1040 1045 1050
Leu Ala Pro Asn Gln Glu Glu Val Arg Ser Ile Lys Ser Glu Thr
1055 1060 1065
Asp Ser Thr Ile Glu Val Asp Ser Val Ala Gly Glu Leu Gln Asp
1070 1075 1080
Leu Gln Ser Glu Gly Asn Ser Ser Pro Ala Gly Phe Asp Ala Ser
1085 1090 1095
Val Ser Ser Ser Ser Ser Asn Gln Pro Glu Pro Glu His Pro Glu
1100 1105 1110
Lys Ala Cys Thr Gly Gln Lys Arg Val Lys Asp Ala Gln Gly Gly
1115 1120 1125
Gly Ser Ser Ser Lys Lys Gln Lys Arg Ser His Lys Ala Thr Val
1130 1135 1140
Val Asn Asn Lys Lys Lys Gly Lys Gly Thr Asn Ser Ser Asp Ser
1145 1150 1155
Glu Glu Leu Ser Ala Gly Glu Ser Ile Thr Lys Ser Gln Pro Val
1160 1165 1170
Lys Ser Val Ser Thr Gly Met Lys Ser His Ser Thr Lys Ser Pro
1175 1180 1185
Ala Arg Thr Gln Ser Pro Gly Lys Cys Gly Lys Asn Gly Asp Lys
1190 1195 1200
Asp Pro Asp Leu Lys Glu Pro Ser Asn Arg Leu Pro Lys Val Tyr
1205 1210 1215
Lys Trp Ser Phe Gln Met Ser Asp Leu Glu Asn Met Thr Ser Ala
1220 1225 1230
Glu Arg Ile Thr Ile Leu Gln Glu Lys Leu Gln Glu Ile Arg Lys

```
                1235                    1240                    1245
His Tyr Leu Ser Leu Lys Ser Glu Val Ala Ser Ile Asp Arg Arg
                1250                    1255                    1260
Arg Lys Arg Leu Lys Lys Lys Glu Arg Glu Ser Ala Ala Thr Ser
                1265                    1270                    1275
Ser Ser Ser Ser Ser Pro Ser Ser Ser Ser Ile Thr Ala Ala Val
                1280                    1285                    1290
Met Leu Thr Leu Ala Glu Pro Ser Met Ser Ser Ala Ser Gln Asn
                1295                    1300                    1305
Gly Met Ser Val Glu Cys Arg
                1310
```

<210> 96
<211> 504
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4909754CD1

<400> 96

```
Met Ala Trp Val Leu Lys Met Asp Glu Val Ile Glu Ser Gly Leu
  1               5                  10                  15
Val His Asp Phe Asp Ala Ser Leu Ser Gly Ile Gly Gln Glu Leu
                 20                  25                  30
Gly Ala Gly Ala Tyr Ser Met Ser Asp Val Leu Ala Leu Pro Ile
                 35                  40                  45
Phe Lys Gln Glu Asp Ser Ser Leu Pro Leu Asp Gly Glu Thr Glu
                 50                  55                  60
His Pro Pro Phe Gln Tyr Val Met Cys Ala Ala Thr Ser Pro Ala
                 65                  70                  75
Val Lys Leu His Asp Glu Thr Leu Thr Tyr Leu Asn Gln Gly Gln
                 80                  85                  90
Ser Tyr Glu Ile Arg Met Leu Asp Asn Arg Lys Met Gly Asp Met
                 95                 100                 105
Pro Glu Ile Ser Gly Lys Leu Val Lys Ser Ile Ile Arg Val Val
                110                 115                 120
Phe His Asp Arg Arg Leu Gln Tyr Thr Glu His Gln Gln Leu Glu
                125                 130                 135
Gly Trp Lys Trp Asn Arg Pro Gly Asp Arg Leu Leu Asp Leu Asp
                140                 145                 150
Ile Pro Met Ser Val Gly Ile Ile Asp Thr Arg Thr Asn Pro Ser
                155                 160                 165
Gln Leu Asn Ala Val Glu Phe Leu Trp Asp Pro Ala Lys Arg Thr
                170                 175                 180
Ser Ala Phe Ile Gln Val His Cys Ile Ser Thr Glu Phe Thr Pro
                185                 190                 195
Arg Lys His Gly Gly Glu Lys Gly Val Pro Phe Arg Ile Gln Val
                200                 205                 210
Asp Thr Phe Lys Gln Asn Glu Asn Gly Glu Tyr Thr Asp His Leu
                215                 220                 225
His Ser Ala Ser Cys Gln Ile Lys Val Phe Lys Pro Lys Gly Ala
                230                 235                 240
Asp Arg Lys Gln Lys Thr Asp Arg Glu Lys Met Glu Lys Arg Thr
                245                 250                 255
Ala His Glu Lys Glu Lys Tyr Gln Pro Ser Tyr Asp Thr Thr Ile
                260                 265                 270
Leu Thr Glu Cys Ser Pro Trp Pro Asp Ala Pro Thr Ala Tyr Val
                275                 280                 285
Asn Asn Ser Pro Ser Pro Ala Pro Thr Phe Thr Ser Pro Gln Gln
                290                 295                 300
Ser Thr Cys Ser Val Pro Asp Ser Asn Ser Ser Ser Pro Asn His
```

```
                305                           310                           315
Gln Gly Asp Gly Ala Ser Gln Thr Ser Gly Glu Gln Ile Gln Pro
                320                           325                           330
Ser Ala Thr Ile Gln Glu Thr Gln Gln Trp Leu Leu Lys Asn Arg
                335                           340                           345
Phe Ser Ser Tyr Thr Arg Leu Phe Ser Asn Phe Ser Gly Ala Asp
                350                           355                           360
Leu Leu Lys Leu Thr Lys Glu Asp Leu Val Gln Ile Cys Gly Ala
                365                           370                           375
Ala Asp Gly Ile Arg Leu Tyr Asn Ser Leu Lys Ser Arg Ser Val
                380                           385                           390
Arg Pro Arg Leu Thr Ile Tyr Val Cys Arg Glu Gln Pro Ser Ser
                395                           400                           405
Thr Val Leu Gln Gly Gln Gln Gln Ala Ala Ser Ser Ala Ser Glu
                410                           415                           420
Asn Gly Ser Gly Ala Pro Tyr Val Tyr His Ala Ile Tyr Leu Glu
                425                           430                           435
Glu Met Ile Ala Ser Glu Val Ala Arg Lys Leu Ala Leu Val Phe
                440                           445                           450
Asn Ile Pro Leu His Gln Ile Asn Gln Val Tyr Arg Gln Gly Pro
                455                           460                           465
Thr Gly Ile His Ile Leu Val Ser Asp Gln Met Val Gln Asn Phe
                470                           475                           480
Gln Asp Glu Ser Cys Phe Leu Phe Ser Thr Val Lys Ala Glu Ser
                485                           490                           495
Ser Asp Gly Ile His Ile Ile Leu Lys
                500
```

<210> 97
<211> 227
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4911931CD1

<400> 97

```
Met Phe Lys Arg Met Ala Glu Phe Gly Pro Asp Ser Gly Gly Arg
  1               5                            10                           15
Val Lys Gly Val Thr Ile Val Lys Pro Ile Val Tyr Gly Asn Val
                 20                            25                           30
Ala Arg Tyr Phe Gly Lys Lys Arg Glu Glu Asp Gly His Thr His
                 35                            40                           45
Gln Trp Thr Val Tyr Val Lys Pro Tyr Arg Asn Glu Asp Met Ser
                 50                            55                           60
Ala Tyr Val Lys Lys Ile Gln Phe Lys Leu His Glu Ser Tyr Gly
                 65                            70                           75
Asn Pro Leu Arg Val Val Thr Lys Pro Pro Tyr Glu Ile Thr Glu
                 80                            85                           90
Thr Gly Trp Gly Glu Phe Glu Ile Ile Ile Lys Ile Phe Phe Ile
                 95                           100                          105
Asp Pro Asn Glu Arg Pro Val Thr Leu Tyr His Leu Leu Lys Leu
                110                           115                          120
Phe Gln Ser Asp Thr Asn Ala Met Leu Gly Lys Lys Thr Val Val
                125                           130                          135
Ser Glu Phe Tyr Asp Glu Met Ile Phe Gln Asp Pro Thr Ala Met
                140                           145                          150
Met Gln Gln Leu Leu Thr Thr Ser Arg Gln Leu Thr Leu Gly Ala
                155                           160                          165
Tyr Lys His Glu Thr Glu Phe Ala Glu Leu Glu Val Lys Thr Arg
                170                           175                          180
Glu Lys Leu Glu Ala Ala Lys Lys Lys Thr Ser Phe Glu Ile Ala
```

```
                185                 190                 195
Glu Leu Lys Glu Arg Leu Lys Ala Ser Arg Glu Thr Ile Asn Cys
                200                 205                 210
Leu Lys Asn Glu Ile Arg Lys Leu Glu Glu Asp Asp Gln Ala Lys
                215                 220                 225
Asp Ile
```

<210> 98
<211> 233
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 4920433CD1

<400> 98

```
Met Ala Glu Asp Gly Leu Pro Lys Ile Tyr Ser His Pro Pro Thr
  1               5                  10                  15
Glu Ser Ser Lys Thr Pro Thr Ala Ala Thr Ile Phe Phe Gly Ala
                 20                  25                  30
Asp Asn Ala Ile Pro Lys Ser Glu Thr Thr Ile Thr Ser Glu Gly
                 35                  40                  45
Asp His Val Thr Ser Val Asn Glu Tyr Met Leu Glu Ser Asp Phe
                 50                  55                  60
Ser Thr Thr Thr Asp Asn Lys Leu Thr Ala Lys Lys Glu Lys Leu
                 65                  70                  75
Lys Ser Glu Asp Asp Met Gly Thr Asp Phe Ile Lys Ser Thr Thr
                 80                  85                  90
His Leu Gln Lys Glu Ile Thr Ser Leu Thr Gly Thr Thr Asn Ser
                 95                 100                 105
Ile Thr Arg Asp Ser Ile Thr Glu His Phe Met Pro Val Lys Ile
                110                 115                 120
Gly Asn Ile Ser Ser Pro Val Thr Thr Val Ser Leu Ile Asp Phe
                125                 130                 135
Ser Thr Asp Ile Ala Lys Glu Asp Ile Leu Leu Ala Thr Ile Asp
                140                 145                 150
Thr Gly Asp Ala Glu Ile Ser Ile Thr Ser Glu Val Ser Gly Thr
                155                 160                 165
Leu Lys Asp Ser Ser Ala Gly Val Ala Asp Ala Pro Ala Phe Pro
                170                 175                 180
Arg Lys Lys Asp Glu Ala Asp Met Ser Asn Tyr Asn Ser Ser Ile
                185                 190                 195
Lys Ser Asn Val Pro Ala Asp Glu Ala Val Gln Val Thr Asp Ser
                200                 205                 210
Ile Ile Pro Glu Ala Glu Ile Leu Leu Leu Leu Lys Lys Pro His
                215                 220                 225
Tyr Tyr Ser Arg His Asn Cys Pro
                230
```

<210> 99
<211> 511
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5042113CD1

<400> 99

```
Met Asp Glu Glu Ser Leu Glu Ser Ala Leu Gln Thr Tyr Arg Ala
  1               5                  10                  15
```

Gln Leu Gln Gln Val Glu Leu Ala Leu Gly Ala Gly Leu Asp Ser
20 25 30
Ser Glu Gln Ala Asp Leu Arg Gln Leu Gln Gly Asp Leu Lys Glu
35 40 45
Leu Ile Glu Leu Thr Glu Ala Ser Leu Val Ser Val Arg Lys Ser
50 55 60
Arg Leu Leu Ala Ala Leu Asp Glu Glu Arg Pro Gly Arg Gln Glu
65 70 75
Asp Ala Glu Tyr Gln Ala Phe Arg Glu Ala Ile Thr Glu Ala Val
80 85 90
Glu Ala Pro Ala Ala Ala Arg Gly Ser Gly Ser Glu Thr Val Pro
95 100 105
Lys Ala Glu Ala Gly Pro Glu Ser Ala Ala Gly Gly Gln Glu Glu
110 115 120
Glu Glu Gly Glu Asp Glu Glu Glu Leu Ser Gly Thr Lys Val Ser
125 130 135
Ala Pro Tyr Tyr Ser Ser Trp Gly Thr Leu Glu Tyr His Asn Ala
140 145 150
Met Val Val Gly Thr Glu Glu Ala Glu Asp Gly Ser Ala Gly Val
155 160 165
Arg Val Leu Tyr Leu Tyr Pro Thr His Lys Ser Leu Lys Pro Cys
170 175 180
Pro Phe Phe Leu Glu Gly Lys Cys Arg Phe Lys Glu Asn Cys Arg
185 190 195
Phe Ser His Gly Gln Val Val Ser Leu Asp Glu Leu Arg Pro Phe
200 205 210
Gln Asp Pro Asp Leu Ser Ser Leu Gln Ala Gly Ser Ala Cys Leu
215 220 225
Ala Lys His Gln Asp Gly Leu Trp His Ala Ala Arg Ile Thr Asp
230 235 240
Val Asp Asn Gly Tyr Tyr Thr Val Lys Phe Asp Ser Leu Leu Leu
245 250 255
Arg Glu Ala Val Val Glu Gly Asp Gly Ile Leu Pro Pro Leu Arg
260 265 270
Thr Glu Ala Thr Glu Ser Asp Ser Asp Ser Asp Gly Thr Gly Asp
275 280 285
Ser Ser Tyr Ala Arg Val Val Gly Ser Asp Ala Val Asp Ser Gly
290 295 300
Thr Cys Ser Ser Ala Phe Ala Gly Trp Glu Val His Thr Arg Gly
305 310 315
Ile Gly Ser Arg Leu Leu Thr Lys Met Gly Tyr Glu Phe Gly Lys
320 325 330
Gly Leu Gly Arg His Ala Glu Gly Arg Val Glu Pro Ile His Ala
335 340 345
Val Val Leu Pro Arg Gly Lys Ser Leu Asp Gln Cys Val Glu Thr
350 355 360
Leu Gln Lys Gln Thr Arg Val Gly Lys Ala Gly Thr Asn Lys Pro
365 370 375
Pro Arg Cys Arg Gly Arg Gly Ala Arg Pro Gly Gly Arg Pro Ala
380 385 390
Pro Arg Asn Val Phe Asp Phe Leu Asn Glu Lys Leu Gln Gly Gln
395 400 405
Ala Pro Gly Ala Leu Glu Ala Gly Ala Ala Pro Ala Gly Arg Arg
410 415 420
Ser Lys Asp Met Tyr His Ala Ser Lys Ser Ala Lys Arg Ala Leu
425 430 435
Ser Leu Arg Leu Phe Gln Thr Glu Glu Lys Ile Glu Arg Thr Gln
440 445 450
Arg Asp Ile Arg Ser Ile Gln Glu Ala Leu Ala Arg Asn Ala Gly
455 460 465
Arg His Ser Val Ala Ser Ala Gln Leu Gln Glu Lys Leu Ala Gly
470 475 480
Ala Gln Arg Gln Leu Gly Gln Leu Arg Ala Gln Glu Ala Gly Leu

```
                485                     490                     495
Gln Gln Glu Gln Arg Lys Ala Asp Thr His Lys Lys Met Thr Glu
                500                     505                     510
Phe


<210> 100
<211> 247
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5083853CD1

<400> 100
Met Glu Val Leu Glu Ser Gly Glu Gln Gly Val Leu Gln Trp Asp
  1               5                  10                  15
Arg Lys Leu Ser Glu Leu Ser Glu Pro Gly Asp Gly Glu Ala Leu
                 20                  25                  30
Met Tyr His Thr His Phe Ser Glu Leu Leu Asp Glu Phe Ser Gln
                 35                  40                  45
Asn Val Leu Gly Gln Leu Leu Asn Asp Pro Phe Leu Ser Glu Lys
                 50                  55                  60
Ser Val Ser Met Glu Val Glu Pro Ser Pro Thr Ser Pro Ala Pro
                 65                  70                  75
Leu Ile Gln Ala Glu His Ser Tyr Ser Leu Cys Glu Glu Pro Arg
                 80                  85                  90
Ala Gln Ser Pro Phe Thr His Ile Thr Ser Asp Ser Phe Asn Asp
                 95                 100                 105
Asp Glu Val Glu Ser Glu Lys Trp Tyr Leu Ser Thr Asp Phe Pro
                110                 115                 120
Ser Thr Ser Ile Lys Thr Glu Pro Ile Thr Asp Glu Pro Pro Pro
                125                 130                 135
Gly Leu Val Pro Ser Val Thr Leu Thr Ile Thr Ala Ile Ser Thr
                140                 145                 150
Pro Leu Glu Lys Glu Glu Pro Pro Leu Glu Met Asn Thr Gly Val
                155                 160                 165
Asp Ser Ser Cys Gln Thr Ile Ile Pro Lys Ile Lys Leu Glu Pro
                170                 175                 180
His Glu Val Asp Gln Phe Leu Asn Phe Ser Pro Lys Glu Gly Leu
                185                 190                 195
Ser Ala Leu Pro Val Ser Leu Trp Val Met Asp Met Val Ser Gly
                200                 205                 210
Ser Thr Glu Arg Glu Tyr Gly Glu Arg Ala Gly Met Ser Leu Tyr
                215                 220                 225
His Arg Cys Cys Ser Trp Leu Tyr Glu Ile Ala Leu Phe Leu Lys
                230                 235                 240
Asn Lys Asn Phe Ala Ser Lys
                245

<210> 101
<211> 276
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5283981CD1

<400> 101
Met Gly Ser Lys Ala Leu Pro Ala Pro Ile Pro Leu His Pro Ser
  1               5                  10                  15
```

Leu Gln Leu Thr Asn Tyr Ser Phe Leu Gln Ala Val Asn Thr Phe
20 25 30
Pro Ala Thr Val Asp His Leu Gln Gly Leu Tyr Gly Leu Ser Ala
35 40 45
Val Gln Thr Met His Met Asn His Trp Thr Leu Gly Tyr Pro Asn
50 55 60
Val His Glu Ile Thr Arg Ser Thr Ile Thr Glu Met Ala Ala Ala
65 70 75
Gln Gly Leu Val Asp Ala Arg Phe Pro Phe Pro Ala Leu Pro Phe
80 85 90
Thr Thr His Leu Phe His Pro Lys Gln Gly Ala Ile Ala His Val
95 100 105
Leu Pro Ala Leu His Lys Asp Arg Pro Arg Phe Asp Phe Ala Asn
110 115 120
Leu Ala Val Ala Ala Thr Gln Glu Asp Pro Pro Lys Met Gly Asp
125 130 135
Leu Ser Lys Leu Ser Pro Gly Leu Gly Ser Pro Ile Ser Gly Leu
140 145 150
Ser Lys Leu Thr Pro Asp Arg Lys Pro Ser Arg Gly Arg Leu Pro
155 160 165
Ser Lys Thr Lys Lys Glu Phe Ile Cys Lys Phe Cys Gly Arg His
170 175 180
Phe Thr Lys Ser Tyr Asn Leu Leu Ile His Glu Arg Thr His Thr
185 190 195
Asp Glu Arg Pro Tyr Thr Cys Asp Ile Cys His Lys Ala Phe Arg
200 205 210
Arg Gln Asp His Leu Arg Asp His Arg Tyr Ile His Ser Lys Glu
215 220 225
Lys Pro Phe Lys Cys Gln Glu Cys Gly Lys Gly Phe Cys Gln Ser
230 235 240
Arg Thr Leu Ala Val His Lys Thr Leu His Met Gln Thr Ser Ser
245 250 255
Pro Thr Ala Ala Ser Ser Ala Ala Lys Cys Ser Gly Glu Thr Val
260 265 270
Ile Cys Gly Gly Thr Ala
275

<210> 102
<211> 220
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5510549CD1

<400> 102
Met Pro Leu Gln Arg Leu Asp Asn Asp Val Asp Leu Arg Gly Asp
1 5 10 15
Gln Pro Ser Leu Gly Ser Phe Thr Tyr Ser Thr Ser Ala Pro Gly
20 25 30
Pro Ala Leu Ser Pro Ser Val Pro Leu His Tyr Leu Pro His Asp
35 40 45
Pro Leu His Gln Glu Leu Ser Phe Gly Val Pro Tyr Ser His Met
50 55 60
Met Pro Arg Arg Leu Ser Thr Gln Arg Tyr Arg Leu Gln Gln Pro
65 70 75
Leu Pro Pro Pro Pro Pro Pro Pro Pro Pro Pro Pro Tyr Tyr Pro
80 85 90
Ser Phe Leu Pro Tyr Phe Leu Ser Met Leu Pro Met Ser Pro Thr
95 100 105
Ala Met Gly Pro Thr Ile Ser Leu Asp Leu Asp Val Asp Asp Val
110 115 120

```
Glu Met Glu Asn Tyr Glu Ala Leu Leu Asn Leu Ala Glu Arg Leu
                125                 130                 135
Gly Asp Ala Lys Pro Arg Gly Leu Thr Lys Ala Asp Ile Glu Gln
                140                 145                 150
Leu Pro Ser Tyr Arg Phe Asn Pro Asp Ser His Gln Ser Glu Gln
                155                 160                 165
Thr Leu Cys Val Val Cys Phe Ser Asp Phe Glu Ala Arg Gln Leu
                170                 175                 180
Leu Arg Val Leu Pro Cys Asn His Glu Phe His Thr Lys Cys Val
                185                 190                 195
Asp Lys Trp Leu Lys Ala Asn Arg Thr Cys Pro Ile Cys Arg Ala
                200                 205                 210
Asp Ala Ser Glu Val Pro Arg Glu Ala Glu
                215                 220

<210> 103
<211> 608
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5544862CD1

<400> 103
Met Asp Thr Glu Glu Arg Lys Asp Lys Asp Ser Ile His Gly His
  1               5                  10                  15
Ser Gln Leu Asp Lys Arg Pro Glu Pro Ser Thr Leu Glu Asn Ile
                 20                  25                  30
Thr Asp Asp Lys Tyr Ala Thr Val Ser Ser Pro Ser Lys Ser Lys
                 35                  40                  45
Lys Leu Glu Cys Pro Ser Pro Ala Glu Gln Lys Pro Ala Glu His
                 50                  55                  60
Val Ser Leu Ser Asn Pro Ala Pro Leu Leu Val Ser Pro Glu Val
                 65                  70                  75
His Leu Thr Pro Ala Val Pro Ser Leu Pro Ala Thr Val Pro Ala
                 80                  85                  90
Trp Pro Ser Glu Pro Thr Thr Phe Gly Pro Thr Gly Val Pro Ala
                 95                 100                 105
Pro Ile Pro Val Leu Ser Val Thr Gln Thr Leu Thr Thr Gly Pro
                110                 115                 120
Asp Ser Ala Val Ser Gln Ala His Leu Thr Pro Ser Pro Val Pro
                125                 130                 135
Val Ser Ile Gln Ala Val Asn Gln Pro Leu Met Pro Leu Pro Gln
                140                 145                 150
Thr Leu Ser Leu Tyr Gln Asp Pro Leu Tyr Pro Gly Phe Pro Cys
                155                 160                 165
Asn Glu Lys Gly Asp Arg Ala Ile Val Pro Pro Tyr Ser Leu Cys
                170                 175                 180
Gln Thr Gly Glu Asp Leu Pro Lys Asp Lys Asn Ile Leu Arg Phe
                185                 190                 195
Phe Phe Asn Leu Gly Val Lys Ala Tyr Ser Cys Pro Met Trp Ala
                200                 205                 210
Pro His Ser Tyr Leu Tyr Pro Leu His Gln Ala Tyr Leu Ala Ala
                215                 220                 225
Cys Arg Met Tyr Pro Lys Val Pro Val Pro Val Tyr Pro His Asn
                230                 235                 240
Pro Trp Phe Gln Glu Ala Pro Ala Ala Gln Asn Glu Ser Asp Cys
                245                 250                 255
Thr Cys Thr Asp Ala His Phe Pro Met Gln Thr Glu Ala Ser Val
                260                 265                 270
Asn Gly Gln Met Pro Gln Pro Glu Ile Gly Pro Pro Thr Phe Ser
                275                 280                 285
```

Ser Pro Leu Val Ile Pro Pro Ser Gln Val Ser Glu Ser His Gly
290 295 300
Gln Leu Ser Tyr Gln Ala Asp Leu Glu Ser Glu Thr Pro Gly Gln
305 310 315
Leu Leu His Ala Asp Tyr Glu Glu Ser Leu Ser Gly Lys Asn Met
320 325 330
Phe Pro Gln Pro Ser Phe Gly Pro Asn Pro Phe Leu Gly Pro Val
335 340 345
Pro Ile Ala Pro Pro Phe Phe Pro His Val Trp Tyr Gly Tyr Pro
350 355 360
Phe Gln Gly Phe Ile Glu Asn Pro Val Met Arg Gln Asn Ile Val
365 370 375
Leu Pro Ser Asp Glu Lys Gly Glu Leu Asp Leu Ser Leu Glu Asn
380 385 390
Leu Asp Leu Ser Lys Asp Cys Gly Ser Val Ser Thr Val Asp Glu
395 400 405
Phe Pro Glu Ala Arg Gly Glu His Val His Ser Leu Pro Glu Ala
410 415 420
Ser Val Ser Ser Lys Pro Asp Glu Gly Arg Thr Glu Gln Ser Ser
425 430 435
Gln Thr Arg Lys Ala Asp Thr Ala Leu Ala Ser Ile Pro Pro Val
440 445 450
Ala Glu Gly Lys Ala His Pro Pro Thr Gln Ile Leu Asn Arg Glu
455 460 465
Arg Glu Thr Val Pro Val Glu Leu Glu Pro Lys Arg Thr Ile Gln
470 475 480
Ser Leu Lys Glu Lys Lys Lys Lys Val Lys Asp Pro Lys Thr Ala
485 490 495
Ala Asp Val Val Ser Pro Gly Ala Asn Ser Val Asp Ser Arg Val
500 505 510
Gln Arg Pro Lys Glu Glu Ser Ser Glu Asp Glu Asn Glu Val Ser
515 520 525
Asn Ile Leu Arg Ser Gly Arg Ser Lys Gln Phe Tyr Asn Gln Thr
530 535 540
Tyr Gly Ser Arg Lys Tyr Lys Ser Asp Trp Gly Tyr Ser Gly Arg
545 550 555
Gly Gly Tyr Gln His Val Arg Ser Glu Glu Ser Trp Lys Gly Gln
560 565 570
Pro Ser Arg Ser Arg Asp Glu Gly Tyr Gln Tyr His Arg Asn Val
575 580 585
Arg Gly Arg Pro Phe Arg Gly Asp Arg Arg Arg Ser Gly Met Gly
590 595 600
Asp Gly His Arg Gly Gln His Thr
605

<210> 104
<211> 653
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5573394CD1

<400> 104
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Ile Val Ser Ile Leu Asn Tyr Val Ile Tyr Lys Asn Thr His Ile
20 25 30
Lys Thr Val Ala Ile Pro Ala Leu Ser Ser Gly Ile Phe Gln Phe
35 40 45
Pro Leu Asn Leu Cys Thr Lys Thr Ile Val Glu Thr Ile Arg Val
50 55 60

Ser Leu Gln Gly Lys Pro Met Met Ser Asn Leu Lys Glu Ile His
65 70 75
Leu Val Ser Asn Glu Asp Pro Thr Val Ala Ala Phe Lys Ala Ala
80 85 90
Ser Glu Phe Ile Leu Gly Lys Ser Glu Leu Gly Gln Glu Thr Thr
95 100 105
Pro Ser Phe Asn Ala Met Val Val Asn Asn Leu Thr Leu Gln Ile
110 115 120
Val Gln Gly His Ile Glu Trp Gln Thr Ala Asp Val Ile Val Asn
125 130 135
Ser Val Asn Pro His Asp Ile Thr Val Gly Pro Val Ala Lys Ser
140 145 150
Ile Leu Gln Gln Ala Gly Val Glu Met Lys Ser Glu Phe Leu Ala
155 160 165
Thr Lys Ala Lys Gln Phe Gln Arg Ser Gln Leu Val Leu Val Thr
170 175 180
Lys Gly Phe Asn Leu Phe Cys Lys Tyr Ile Tyr His Val Leu Trp
185 190 195
His Ser Glu Phe Pro Lys Pro Gln Ile Leu Lys His Ala Met Lys
200 205 210
Glu Cys Leu Glu Lys Cys Ile Glu Gln Asn Ile Thr Ser Ile Ser
215 220 225
Phe Pro Ala Leu Gly Thr Gly Asn Met Glu Ile Lys Lys Glu Thr
230 235 240
Ala Ala Glu Ile Leu Phe Asp Glu Val Leu Thr Phe Ala Lys Asp
245 250 255
His Val Lys His Gln Leu Thr Val Lys Phe Val Ile Phe Pro Thr
260 265 270
Asp Leu Glu Ile Tyr Lys Ala Phe Ser Ser Glu Met Ala Lys Arg
275 280 285
Ser Lys Met Leu Ser Leu Asn Asn Tyr Ser Val Pro Gln Ser Thr
290 295 300
Arg Glu Glu Lys Arg Glu Asn Gly Leu Glu Ala Arg Ser Pro Ala
305 310 315
Ile Asn Leu Met Gly Phe Asn Val Glu Glu Met Cys Glu Ala His
320 325 330
Ala Trp Ile Gln Arg Ile Leu Ser Leu Gln Asn His His Ile Ile
335 340 345
Glu Asn Asn His Ile Leu Tyr Leu Gly Arg Lys Glu His Asp Ile
350 355 360
Leu Ser Gln Leu Gln Lys Thr Ser Ser Val Ser Ile Thr Glu Ile
365 370 375
Ile Ser Pro Gly Arg Thr Glu Leu Glu Ile Glu Gly Ala Arg Ala
380 385 390
Asp Leu Ile Glu Val Val Met Asn Ile Glu Asp Met Leu Cys Lys
395 400 405
Val Gln Glu Glu Met Ala Arg Lys Lys Glu Arg Gly Leu Trp Arg
410 415 420
Ser Leu Gly Gln Trp Thr Ile Gln Gln Gln Lys Thr Gln Asp Glu
425 430 435
Met Lys Glu Asn Ile Ile Phe Leu Lys Cys Pro Val Pro Pro Thr
440 445 450
Gln Glu Leu Leu Asp Gln Lys Lys Gln Phe Glu Lys Cys Gly Leu
455 460 465
Gln Val Leu Lys Val Glu Lys Ile Asp Asn Glu Val Leu Met Ala
470 475 480
Ala Phe Gln Arg Lys Lys Lys Met Met Glu Glu Lys Leu His Arg
485 490 495
Gln Pro Val Ser His Arg Leu Phe Gln Gln Val Pro Tyr Gln Phe
500 505 510
Cys Asn Val Val Cys Arg Val Gly Phe Gln Arg Met Tyr Ser Thr
515 520 525
Pro Cys Asp Pro Lys Tyr Gly Ala Gly Ile Tyr Phe Thr Lys Asn

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                    530                       535                       540
Leu Lys Asn Leu Ala Glu Lys Ala Lys Lys Ile Ser Ala Ala Asp
                    545                       550                       555
Lys Leu Ile Tyr Val Phe Glu Ala Glu Val Leu Thr Gly Phe Phe
                    560                       565                       570
Cys Gln Gly His Pro Leu Asn Ile Val Pro Pro Pro Leu Ser Pro
                    575                       580                       585
Gly Ala Ile Asp Gly His Asp Ser Val Val Asp Asn Val Ser Ser
                    590                       595                       600
Pro Glu Thr Phe Val Ile Phe Ser Gly Met Gln Ala Ile Pro Gln
                    605                       610                       615
Tyr Leu Trp Thr Cys Thr Gln Glu Tyr Val Gln Ser Gln Asp Tyr
                    620                       625                       630
Ser Ser Gly Pro Met Arg Pro Phe Ala Gln His Pro Trp Arg Gly
                    635                       640                       645
Phe Ala Ser Gly Ser Pro Val Asp
                    650

<210> 105
<211> 154
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5850840CD1

<400> 105
Met Gly Asn Cys Leu Lys Ser Pro Thr Ser Asp Asp Ile Ser Leu
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Leu His Glu Ser Gln Ser Asp Arg Ala Ser Phe Gly Glu Gly Thr
                    20                       25                       30
Glu Pro Asp Gln Glu Pro Pro Pro Pro Tyr Gln Glu Gln Val Pro
                    35                       40                       45
Val Pro Val Tyr His Pro Thr Pro Ser Gln Thr Arg Leu Ala Thr
                    50                       55                       60
Gln Leu Thr Glu Glu Glu Gln Ile Arg Ile Ala Gln Arg Ile Gly
                    65                       70                       75
Leu Ile Gln His Leu Pro Lys Gly Val Tyr Asp Pro Gly Arg Asp
                    80                       85                       90
Gly Ser Glu Lys Lys Ile Arg Glu Cys Val Ile Cys Met Met Asp
                    95                       100                      105
Phe Val Tyr Gly Asp Pro Ile Arg Phe Leu Pro Cys Met His Ile
                    110                      115                      120
Tyr His Leu Asp Cys Ile Asp Asp Trp Leu Met Arg Ser Phe Thr
                    125                      130                      135
Cys Pro Ser Cys Met Glu Pro Val Asp Ala Ala Leu Leu Ser Ser
                    140                      145                      150
Tyr Glu Thr Asn


<210> 106
<211> 337
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5942936CD1

<400> 106
Met Lys Arg Pro Cys Glu Glu Thr Thr Ser Glu Ser Asp Met Asp
  1                 5                        10                       15
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Glu Thr Ile Asp Val Gly Ser Glu Asn Asn Tyr Ser Gly Gln Ser
20 25 30
Thr Ser Ser Val Ile Arg Leu Asn Ser Pro Thr Thr Thr Ser Gln
35 40 45
Ile Met Ala Arg Lys Lys Arg Arg Gly Ile Ile Glu Lys Arg Arg
50 55 60
Arg Asp Arg Ile Asn Asn Ser Leu Ser Glu Leu Arg Arg Leu Val
65 70 75
Pro Thr Ala Phe Glu Lys Gln Gly Ser Ala Lys Leu Glu Lys Ala
80 85 90
Glu Ile Leu Gln Met Thr Val Asp His Leu Lys Met Leu Gln Ala
95 100 105
Thr Gly Gly Lys Gly Tyr Phe Asp Ala His Ala Leu Ala Met Asp
110 115 120
Phe Met Ser Ile Gly Phe Arg Glu Cys Leu Thr Glu Val Ala Arg
125 130 135
Tyr Leu Ser Ser Val Glu Gly Leu Asp Ser Ser Asp Pro Leu Arg
140 145 150
Val Arg Leu Val Ser His Leu Ser Thr Cys Ala Thr Gln Arg Glu
155 160 165
Ala Ala Ala Met Thr Ser Ser Met Ala His His His His Pro Leu
170 175 180
His Pro His His Trp Ala Ala Ala Phe His His Leu Pro Ala Ala
185 190 195
Leu Leu Gln Pro Asn Gly Leu His Ala Ser Glu Ser Thr Pro Cys
200 205 210
Arg Leu Ser Thr Thr Ser Glu Val Pro Pro Ala His Gly Ser Ala
215 220 225
Leu Leu Thr Ala Thr Phe Ala His Ala Asp Ser Ala Leu Arg Met
230 235 240
Pro Ser Thr Gly Ser Val Ala Pro Cys Val Pro Pro Leu Ser Thr
245 250 255
Ser Leu Leu Ser Leu Ser Ala Thr Val His Ala Ala Ala Ala Ala
260 265 270
Ala Thr Ala Ala Ala His Ser Phe Pro Leu Ser Phe Ala Gly Ala
275 280 285
Phe Pro Met Leu Pro Pro Asn Ala Ala Ala Ala Val Ala Ala Ala
290 295 300
Thr Ala Ile Ser Pro Pro Leu Ser Val Ser Ala Thr Ser Ser Pro
305 310 315
Gln Gln Thr Ser Ser Gly Thr Asn Asn Lys Pro Tyr Arg Pro Trp
320 325 330
Gly Thr Glu Val Gly Ala Phe
335

<210> 107
<211> 535
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 5951431CD1

<400> 107
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1 5 10 15
Arg Leu Arg Ala Val Pro Thr Asn Lys Ala Cys Phe Asp Cys Gly
20 25 30
Ala Lys Asn Pro Ser Trp Ala Ser Ile Thr Tyr Gly Val Phe Leu
35 40 45
Cys Ile Asp Cys Ser Gly Val His Arg Ser Leu Gly Val His Leu
50 55 60

Ser Phe Ile Arg Ser Thr Glu Leu Asp Ser Asn Trp Asn Trp Phe
65 70 75
Gln Leu Arg Cys Met Gln Val Gly Gly Asn Ala Asn Ala Thr Ala
80 85 90
Phe Phe Arg Gln His Gly Cys Thr Ala Asn Asp Ala Asn Thr Lys
95 100 105
Tyr Asn Ser Arg Ala Ala Gln Met Tyr Arg Glu Lys Ile Arg Gln
110 115 120
Leu Gly Ser Ala Ala Leu Ala Arg His Gly Thr Asp Leu Trp Ile
125 130 135
Asp Asn Met Ser Ser Ala Val Pro Asn His Ser Pro Glu Lys Lys
140 145 150
Asp Ser Asp Phe Phe Thr Glu His Thr Gln Pro Pro Ala Trp Asp
155 160 165
Ala Pro Ala Thr Glu Pro Ser Gly Thr Gln Gln Pro Ala Pro Ser
170 175 180
Thr Glu Ser Ser Gly Leu Ala Gln Pro Glu His Gly Pro Asn Thr
185 190 195
Asp Leu Leu Gly Thr Ser Pro Lys Ala Ser Leu Glu Ser Val Tyr
200 205 210
Leu Ser Ala Lys Gly Ala Leu Pro Ala Arg Glu Leu Lys Ser Ser
215 220 225
Ile Ile Gly Lys Lys Lys Pro Ala Ala Ala Lys Lys Gly Leu Gly
230 235 240
Ala Lys Lys Gly Leu Gly Ala Gln Lys Val Ser Ser Gln Ser Phe
245 250 255
Ser Glu Ile Glu Arg Gln Ala Gln Val Ala Glu Lys Leu Arg Glu
260 265 270
Gln Gln Ala Ala Asp Ala Lys Lys Gln Ala Glu Glu Ser Met Val
275 280 285
Ala Ser Met Arg Leu Ala Tyr Gln Glu Leu Gln Ile Asp Arg Lys
290 295 300
Lys Glu Glu Lys Lys Leu Gln Asn Leu Glu Gly Lys Lys Arg Glu
305 310 315
Gln Ala Glu Arg Leu Gly Met Gly Leu Val Ser Arg Ser Ser Val
320 325 330
Ser His Ser Val Leu Ser Glu Met Gln Val Ile Glu Gln Glu Thr
335 340 345
Pro Val Ser Ala Lys Ser Ser Arg Ser Gln Leu Asp Leu Phe Asp
350 355 360
Asp Val Gly Thr Phe Ala Ser Gly Pro Pro Lys Tyr Lys Asp Asn
365 370 375
Pro Phe Ser Leu Gly Glu Ser Phe Gly Ser Arg Trp Asp Thr Asp
380 385 390
Ala Ala Trp Gly Met Asp Arg Val Glu Glu Lys Glu Pro Glu Val
395 400 405
Thr Ile Ser Ser Ile Arg Pro Ile Ser Glu Arg Ala Thr Asn Arg
410 415 420
Arg Glu Val Glu Ser Arg Ser Ser Gly Leu Glu Ser Ser Glu Ala
425 430 435
Arg Gln Lys Phe Ala Gly Ala Lys Ala Ile Ser Ser Asp Met Phe
440 445 450
Phe Gly Arg Glu Val Asp Ala Glu Tyr Glu Ala Arg Ser Arg Leu
455 460 465
Gln Gln Leu Ser Gly Ser Ser Ala Ile Ser Ser Ser Asp Leu Phe
470 475 480
Gly Asp Met Asp Gly Ala His Gly Ala Gly Ser Val Ser Leu Gly
485 490 495
Asn Val Leu Pro Thr Ala Asp Ile Ala Gln Phe Lys Gln Gly Val
500 505 510
Lys Ser Val Ala Gly Lys Met Ala Val Leu Ala Asn Gly Val Met
515 520 525
Asn Ser Leu Gln Asp Arg Tyr Gly Ser Tyr

530 535

<210> 108
<211> 2173
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 095210CB1

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gggccgtgct gggtgcgcgt ttgcaccagt gacgcagccg ctgcatctcc gccagtccgc 120
gcaggccagc atccttcaga aaaagcatcc ccgaggagga agacgaatcg ttaaacatct 180
gaaagggtca ggccagcatc cttcagaaaa agcatccccg aggaggaaga cgaatcgtta 240
aacatcttag gtcagctcta gcctctcgga atttgtcttc ttcagtggaa accccgagaa 300
gactgatcag ttcttcagtt ctaaaacaat ggcccagggt ttggtgacgt tcgccgacgt 360
agccatagac ttttctcagg aggagtgggc ctgtctgaac tctgctcaga gggacctgta 420
ctgggacgtg atgctggaga actacagtaa cttggtctca ctggatttgg agtcagcata 480
tgaaaataag agtttaccta cagaaaaaaa cattcatgaa ataagggctt ccaaaaggaa 540
ttcagataga agaagtaaat cccttggccg taactggata tgtgaaggta cgcttgaaag 600
accacagcgc tccagaggga ggtatgtcaa tcagatgatc atcaattatg tcaaaaggcc 660
tgctactaga gaaggcaccc ctcctagaac acatcagaga catcataagg agaattcctt 720
tgaatgtaag gactgtggga aggcctttag tcgtggctat caacttagtc aacatcagaa 780
aatccatact ggtgagaaac cttatgaatg taaagaatgt aagaaggcct tccgttgggg 840
caatcagctt actcaacatc aaaaaattca tactggggag aagccctacg aatgtaaaga 900
ctgtgggaag gcttttcgat ggggctcaag cctcgttatt cataagagga ttcatactgg 960
tgaaaaaccc tatgaatgta aagactgtgg aaaggccttt cggcgtggtg atgagctcac 1020
tcagcaccag agattccaca ctggggagaa agactacgaa tgcaaagact gtgggaagac 1080
ctttagccgt gtgtataaac ttattcagca caagagaatt catagtgggg agaagcctta 1140
cgagtgtaaa gactgtggga aggcttttat ttgtggttca agcctcattc agcataaaag 1200
aattcacaca ggtgagaaac cctatgaatg tcaagaatgt gggaaggcct ttactcgagt 1260
caattacctt actcagcatc agaagatcca caccggtgag aagcctcacg aatgtaagga 1320
gtgtgggaag gcctttcgct ggggttcgag cctcgttaag cacgagagga tacatacggg 1380
cgagaagccg tacaagtgca cagaatgtgg gaaggccttc aattgtggct atcacctcac 1440
tcagcacgag agaatccaca caggcgaaac cccgtataaa tgtaaggagt gtgggaaggc 1500
tttcatttat ggatcgagcc tcgtgaaaca tgagagaatt cataccgggg tgaaacccta 1560
tgggtgtaca gaatgtggga agagctttag tcacggccat cagcttacac aacatcagaa 1620
aacgcacagt ggggcgaaat cctacgaatg taaggagtgc gggaaggcat gtaaccacct 1680
aaaccatctc cgagaacatc agaggatcca caacagttga agagcctttt gaacgcagta 1740
gcccgctcgt atctatggtt tcgctttcca cagtttgtta cctgcagtca actgcagttc 1800
aaaaatatta aatggaaaat tccagaaata aagaatttta agtctcaaat ggtgtgccct 1860
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tcccttggtc cagcacatcc acgctgtata cgccacccac cctgctagtg acttagtagc 1980
cgtcttggtg atcagatcaa ctatcccagc atcacagtgc ctgtgcccaa gcagtcctca 2040
ctttgcttaa cagtggcccc agagagcagg agtagtgatg ctggtgattc ggatatgcca 2100
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aaaaaaaaaa agg 2173

<210> 109
<211> 1512
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 157953CB1

<400> 109
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ccccccggca ccctccccca accttcccca accccacctg acctggaagc tatggcctcc 120
ctcctcaaga aggagctgga acagatggaa gacttcttcc tagatgcccc gctcctccca 180

ccaccctccc cgccgccact accaccacca ccactaccac cagccccctc cctcccccctg 240
tccctcccct cctttgacct cccccagccc cctgtcttgg atactctgga cttgctggcc 300
atctactgcc gcaacgaggc cgggcaggag gaagtgggga tgccgcctct gcccccgcca 360
cagcagcccc ctcctccttc tccacctcaa ccttctcgcc tggcccccta cccacatcct 420
gccaccaccc gaggggaccg caagcaaaag aagagagacc agaacaagtc ggcggctctg 480
aggtaccgcc agcggaagcg ggcagagggt gaggccctgg agggcgagtg ccagggggctg 540
gaggcacgga atcgcgagct gaaggaacgg gcagagtccg tggagcgcga gatccagtac 600
gtcaaggacc tgctcatcga ggtttacaag gcccggagcc agaggacccg tagctgctag 660
aagggcaggg gtgtggcttc tgggggctgg tcttcagctc tggcgccttc atccccctgc 720
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cactttggga ggccaaggca ggaggatcgt ttgaggccag gaggtcaata ccagcctggg 840
caacatagta agaccctgtc tctattaaaa aaaaaaaatc aaccccttctt ccccaccaaa 900
ccacccaact cctctctact cttatccttt tatcctctgt ctctgcttat cacctctctt 960
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gagcttggaa acctggtctc ttgaatttca aacctggttt cttacaggtg gttgtctggg 1140
gtgggtggag tggcgacagg atagagctga aggactatgc aaatgaggaa gtaagtcagg 1200
gcgggctttg agaaggggac ccatatccta caggcaaaaa gcaggctagg tgaccttggg 1260
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ctaagaaaaa aaatcagtgt ttcgtgaagg tgttggagag gggctgtgtc tgggtgaggg 1440
atggcggggt actgattttt ttgggaggtt atgagcaaaa ataaaacgaa acatttcctc 1500
tgaaaaaaaa aa 1512

<210> 110
<211> 1447
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 159196CB1

<400> 110
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ggagagtgga tgactcagag ggttcttgga tcccacctgg ggagaaggag catgggcaag 180
agagcctgtc ggatgaactg caagaaactc atccaaaaaa gccatggcag aaagtcactg 240
tccgggctcg agagctaggg gaccccattg ctcatccaag gcatgaggca gatgagaagc 300
cctttatatg tgcccagtgt ggcaaaacct tcaataatac ctccaacctg agaacacacc 360
agcggatcca cactggtgag aagccttaca agtgttctga atgtggcaag agcttctcga 420
gaagctccaa ccgcatccgg cacgagcgga tccacctgga agagaaacac tacaaatgcc 480
ccaagtgcca ggagagcttt cggcggcgct cagacctcac cacgcaccag caagatcacc 540
taggcaagcg gccataccgc tgtgacatct gtggcaagag cttcagccag agtgccacgc 600
tagctgtgca tcaccggacc cacctggagc cagcacccta catctgctgt gagtgtggga 660
agagcttcag caacagctcc agctttggcg tgcatcaccg cacccacaca ggtgagagac 720
cttatgagtg cactgagtgt gggcggacct tcagcgatat ctccaacttt ggagcacacc 780
agcggaccca cagaggggag aagccctacc ggtgcactgt gtgtgggaaa cacttctccc 840
ggagctcgaa tctcatccgc caccagaaaa ctcacttggg cgaacaggct gggaaagatt 900
ccagctgaag gagagcccca tttagagtga gggagagaga gtgagagacc ctaacctatt 960
ggaggaagat cttcagcatc ttttgctgct accttgacct caagcccttc atcccacttt 1020
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tggaataaaa acccttgcct ctttccaggc caatttctcg tgttggaaag tcagaagacc 1140
cagtcttggc tttactttct tggggtgaaa gagaaatagg gtaggctcag aacatgctca 1200
tgttattaag gcagcagtcc ccctggcctt tgaggaagta cttatgagat gggtgtcact 1260
gtctgaaggt tctccaaatt gtctgtgaac tgcttaggta ggagtgcact gcagtttcct 1320
gctagttccc acctgttgtg ccccaacttt gcttctagat ctctggggtg ggaggagtga 1380
ccttctcaat ggaagggggcc tccttggtct ggagaagaga tctgaggtcc caccttagaa 1440
atgaaag 1447

<210> 111
<211> 4580
<212> DNA

<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 343338CB1

<400> 111
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gtttgtaagt ggcagtcgtg atgggacagc acgtatttgg caatttaaac gaagagagtg 180
gaagagcatt ttgttggata tggctactcg tccagcaggc caaaaccttc aaggaataga 240
agataaaatc acaaaaatga aggttactat ggtagcttgg gatcgacatg acaatacagt 300
tataactgca gttaataaca tgactctgaa agtttggaat tcttacactg gtcaactaat 360
tcatgtcctg atgggtcatg aagatgaggt atttgttctt gaaccacacc cgttcgatcc 420
tagagttctc ttttctgctg gtcatgatgg aaacgtgata gtgtgggatc tggcaagagg 480
agtcaaaata cgatcttatt tcaatatgat tgaaggccaa ggacatggcg cagtatttga 540
ctgcaaatgc tctcctgatg gtcagcattt tgcatgcaca gactctcatg gacatctttt 600
aatttttggc tttgggtcca gtagcaaata tgacaagata gcagatcaga tgttctttca 660
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gcaagcacct catcttatgc ctcccccttt tttggttgat gttgatggta accctcatcc 780
atcaagatat caaagattag ttcctggccg tgaaaattgc agggaggagc aactcatccc 840
tcagatggga gtaacttcct caggactgaa tcaagtttta agtcagcaag caaaccagga 900
gatcagccca ctggacagca tgattcaaag actacaacag gagcaagacc tgagacgttc 960
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gcaaatgcac agcaacgcac caagaagtga aatagccaca gagcgggatc tggtagcttg 1140
gagtcgaagg gtggtagtac ccgagctatc agctggtgta gccagtaggc aagaagaatg 1200
gagaactgca aagggagaag aagaaataaa gacttacagg tcagaagaga aaagaaaaca 1260
cttaactgtt ccaaaagaga ataaaatacc cactgtctca aagaatcatg ctcatgagca 1320
tttcctggat cttggagaat ccaaaaagca acagacaaat caacacaatt atcgtacaag 1380
atctgcattg gaagagactc ctagaccctc agaagagata gaaaatggca gtagttcttc 1440
agatgaaggc gaagtagttg ctgtcagtgg tggaacatcc gaagaagaag agagagcatg 1500
gcacagtgat ggcagttcta gtgactactc cagtgattac tctgactgga cagcagatgc 1560
aggaattaat ctgcagccac caaagaaagt tcctaagaat aaaaccaaga aagcagaaag 1620
cagttcagat gaagaagaag aatctgaaaa acagaagcaa aaacagatta aaaaggaaaa 1680
gaaaaaagta aatgaagaaa aagatggacc aatatcacca aagaaaaaga agcccaaaga 1740
aagaaaacaa aagagattgg ctgtgggaga actaactgaa aatggtttga cattagaaga 1800
atggttgcca tcaacatgga ttacagatac cattccccga agatgtccat ttgtgccaca 1860
gatgggtgat gaggtttatt atttccgaca aggacatgaa gcctatgtcg aaatggcccg 1920
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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<223> a, t, c, g, or other

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<212> DNA
<213> Homo sapiens

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<211> 2826
<212> DNA
<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

<220>
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<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No: 1234329CB1

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<210> 126
<211> 1956
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1238747CB1

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<211> 1588
<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No: 1265980CB1

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<210> 128
<211> 2205
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1297333CB1

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<220>
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<212> DNA
<213> Homo sapiens

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<213> Homo sapiens

<220>

<221> misc_feature
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<213> Homo sapiens

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<212> DNA
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<210> 141
<211> 3270
<212> DNA
<213> Homo sapiens

<220>
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<210> 142
<211> 1907
<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No: 1609731CB1

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<210> 143
<211> 1800
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1674538CB1

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<210> 144
<211> 1848

<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No: 1675287CB1

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<211> 2056
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1693903CB1

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<213> Homo sapiens

<220>
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<400> 146

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<212> DNA

<213> Homo sapiens

<220>
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<223> Incyte ID No: 1712916CB1

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<213> Homo sapiens

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<213> Homo sapiens

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<223> Incyte ID No: 1842496CB1

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<212> DNA
<213> Homo sapiens

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<212> DNA
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<220>
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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<223> Incyte ID No: 2307537CB1

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<211> 1884
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<213> Homo sapiens

<220>
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<210> 168
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<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No: 2463542CB1

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<211> 1760
<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No: 2486031CB1

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<210> 170
<211> 1965
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2493052CB1

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<210> 171
<211> 2086
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2512074CB1

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<210> 172
<211> 1461
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2646274CB1

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<210> 173
<211> 1066
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2672566CB1

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<210> 174
<211> 1239
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
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<210> 175
<211> 2155
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2703282CB1

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<213> Homo sapiens

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<213> Homo sapiens

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<211> 1685
<212> DNA
<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<211> 1882
<212> DNA
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<212> DNA

<213> Homo sapiens

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